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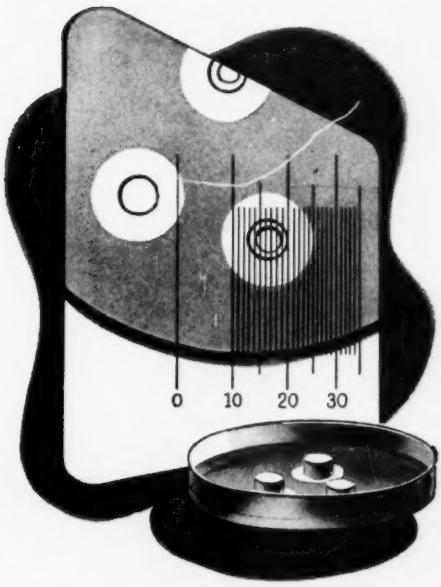

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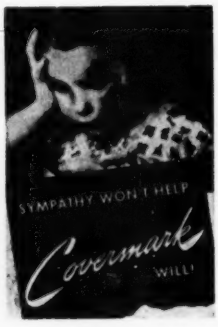

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1 Gross, Elmer R., M.D.; Wright, Carroll S., M.D.; Oral Bismuth Therapy in Syphilis and Various Dermatoses—Paper presented at the Pennsylvania Medical Society Meeting, October 8, 1946 at Philadelphia, Pennsylvania.

2 Gross, Elmer R., M.D.; Howles, James K., M.D.; Non-Specific Treatment of Dermatoses and Adjunctive Therapy of Syphilis with Oral Sodium Bismuth Triglycollamate. Read before the Section of Dermatology and Syphilology Meeting of the Centennial Meeting of the A.M.A. at Atlantic City, New Jersey, June 12, 1947.

3 Year Book of Dermatology and Syphilology, 1946, page 31.

4 Sawicky, H. H., M.D.; Bistrimate (sodium bismuth triglycollamate) Administered by Mouth in the Treatment of Chronic Discoid Lupus Erythematosus. The Journal of Investigative Dermatology, vol. 9 #3 September 1947.

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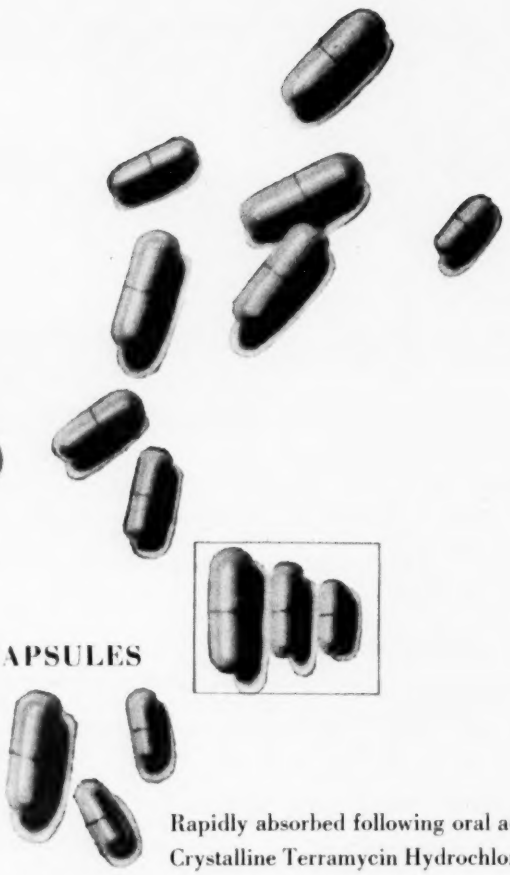

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A. M. A.
Archives of Dermatology and Syphilology

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THE BOUNDARIES OF DERMATOLOGY

Presidential Address

HENRY E. MICHELSON, M.D.
MINNEAPOLIS

THE PIONEERS of dermatology were confronted with the task of analyzing and classifying the many morphologic changes which they observed. They soon learned that certain systemic symptoms accompanied some of the more or less constant morphologic manifestations, and early in the study of dermatology they realized that skin diseases might originate from internal infections or other systemic alterations. Throughout the history of dermatology an effort has been made to correlate external and internal diseases, and with some success. With advances in knowledge the interrelation of the two is becoming more apparent. The skin not only is an organ on which physiologic disturbances are projected, but it has, to a limited degree, its own diseases regulated by its own laws. We, as dermatologists, are interested not only in what internal diseases do to the skin, but also, conversely, in what a severe skin disease, such as a generalized dermatitis, does to the general physiology.

The problems that present themselves when one attempts to visualize the future possibilities of a more intimate knowledge of the connections between the integument and the body as a whole are so great that one can only hope to point out some of the known facts and, from the beginnings that have been made, to imply further investigations that might be pursued. In undertaking such a task, one realizes that dermatology has no boundaries, that it is closely connected with all of the medical specialties. When the dermatologist contemplates a disease, his mental approach is conditioned by his background, but thorough knowledge of that disease must be the sum total of the facts that have been established for it, regardless of their source. Therefore, progress in dermatology can be made only when the skin specialist disregards boundaries, cultivates a receptivity, and maintains a respect for co-workers in all the medical specialties.

Study of infections the origin of which is known, such as syphilis, leprosy, and tuberculosis, offers a good beginning upon which to base an understanding of the reactions of the skin to alterations in allergic and immunologic responses of the organism as a whole. One need only recall the great variation between a syphilitic chancre and a gumma to be impressed with the tremendous influence that acquired resistance plays on a pathologic process. The study of syphilis has provided us with a large store of knowledge concerning its mode of infection, chronology, and immunology. As this disease is brought under control and vanishes over the dermatologic horizon, we must not forget the lessons that have been learned. One of

Read at the Seventy-First Annual Meeting of the American Dermatological Association, Hot Springs, Va., May 23, 1951.

the most fascinating and baffling phenomena which was discovered in the study of syphilis is the ability of the disease to become dormant or latent. This phenomenon, which may occur either naturally or after treatment has failed to eradicate the disease, offers an explanation for its recurrences. The relationship of the organism and the terrain in syphilis leaves many perplexing problems to be explained, but the ability of the body to harbor spirochetes and hold them in check, without destroying them, discloses a principle that probably should be applied to other infections.

The study and the more recent classifications of leprosy have given great impetus to the understanding of its immunobiology. The distinction between lepromatous and tuberculoid leprosy and the facts concerning infectivity and prognosis of the two types have revived hope that their morphology and the associated pathology have a distinct relationship and that such a relationship may also be anticipated in other skin diseases.

In the field of cutaneous tuberculosis many advances in the evolution of our knowledge of the specific granulomas may be pointed out. The information came slowly to dermatology because visual manifestations of disease are bound to be studied first and explained later. The histologic structure of an eruption, its microscopic morphology, becomes significant only when the morphology together with its histology points to the pathogenesis, immunology, and prognosis of the disease. In this regard the cutaneous manifestations of leprosy are more easily understood than those of either syphilis or tuberculosis.

When a remedy is discovered to be more or less specific for a certain disease, an entirely new approach to the study of the disease is offered. The manner in which the tissues react after the causative agent is removed, or rendered static, in a reverse way, may serve to show how the pathologic products accumulated or which structures bore the brunt of the insult of the offending germ and its products. The successful use of calciferol (vitamin D_2) in the treatment of lupus vulgaris has added greatly to our knowledge of tuberculosis. The precise mechanism of its beneficial action is not known, but there may be some parallelism to its action in rickets. If calciferol is given in large but nontoxic doses to a person with normal metabolism, there is no physiologic effect; however, as small a dose as 10 mg. given in florid rickets has a healing effect. Lupus vulgaris, likewise, is a disease which, in addition to infection with a specific bacillus, implies certain metabolic abnormalities that may be caused by deprivation or impaired nutrition. It may be inferred, therefore, that the nonspecific defense has been rendered at least partially incapable of functioning; the skin, which has a very slight disposition for tuberculous infection, is rendered vulnerable, becomes infected, and the specific defense cannot overcome this infection. A source of infection and an altered or impaired nutrition seem to be essential for the development of lupus vulgaris.

When calciferol is given in appropriate dosage to a patient with lupus vulgaris, complete or partial healing of the lesions usually occurs. Whether the healing is due to correction of an altered metabolism or to local action of the vitamin on the diseased tissue, regression of tuberculous inflammation is brought about. The healing process as observed under the microscope reveals a complicated series of changes, occurring in an irregular manner and usually beginning with edema which pries the closely packed epithelioid cells apart. In some cases the lymphocytic

infiltrate disappears first; in others, the epithelioid accumulations are altered and appear to be transformed into fibroblasts. At any rate, the healing of lupus vulgaris under calciferol therapy, in favorable cases, is essentially one of complete or partial regression and alteration of the tuberculous inflammation with fibrous scar formation. Healing rarely begins before the sixth week of treatment, and there is great individuality in its rate of progress. The histologic changes are much slower to regress than the clinical, and complete disappearance of all microscopic signs of inflammation is rare.

The effect of vitamin therapy in this disease throws some light on the source and pathogenesis of lupus vulgaris, for when healing is incomplete following such therapy, it may indicate continued renewal of the infection. It has been my belief that all lupus vulgaris patients have some internal focus of tuberculosis, most likely, pulmonary or glandular. Calciferol has been found to affect glandular tuberculosis favorably but seems to have no beneficial and possibly a detrimental action on pulmonary lesions. However, despite inaction in certain forms of tuberculosis, the vitamin apparently has no direct injurious action on the tubercle bacillus; probably it is not even bacteriostatic. Its effect on lupus vulgaris, admittedly a distinct form of tuberculosis, is rather directly on tissues which, for various reasons, possibly metabolic, became diseased. When these tissues are suffused with calciferol, they are able to bring about partial or at times complete healing with scar formation. The vitamin is, therefore, a means of assisting or reinforcing the defense of a certain tissue against tuberculosis, but to cure the disease the source of the bacilli in the body must be sought and combated by other means. If elimination of the source is not successful, recurrences may and frequently do occur.

If the entire field of cutaneous tuberculosis is considered, it may be appreciated why morphologic differences are dependent, among other things, upon the tuberculous process in the individual patient and, particularly, upon the factors of chronology of infection, body type, nutrition, environment, and possibly heredity. If the source of all cutaneous tuberculosis, except the primary complex, is internal, we must consider all possible associations, such as predisposing factors, the embryonic origin of the involved tissues, and those signs suggested in careful clinical examinations. For example, simultaneous glandular and cutaneous involvement is often observed. One of the oldest recognized forms of tuberculosis was the so-called scrofulosis, a chronic form of glandular and cutaneous tuberculosis. This condition was a scourge in Europe in years gone by and is still seen in primitive peoples living under conditions of chronic malnourishment, such as some American Indians. I bring it into this discussion because lupus vulgaris at times develops about scrofulous sinuses, and in both conditions undernourishment seems to play a role. There seems to be a definite relationship between glandular tuberculosis and lupus vulgaris, as well as some other forms of cutaneous tuberculosis. In fact, clinical or subclinical glandular infection may be a requisite for the development of lupus vulgaris, but this is hard to prove. Nevertheless, observation of patients having scrofuloderma with multiple tissue involvement has shown that when they are treated with calciferol healing of the deeper structures is a prerequisite for healing of the skin lesions. Moreover, in a considerable number of lupus vulgaris patients, superficial glands which were not known to be infected became inflamed (Herxheimer-like reaction) and therefore demonstrable after calciferol therapy was

instituted. These facts strengthen the view that lupus vulgaris and other cutaneous tuberculosis is only a visible manifestation of systemic tuberculosis. Therefore, cutaneous tuberculosis may be interpreted in the same manner as the cutaneous lesions of the other specific granulomas, i. e., syphilis and leprosy. Each disease has its own tempo, its own laws, but the comparisons are valid, and I believe that tuberculosis of the skin cannot be understood if it is regarded as an isolated tissue reaction.

Sarcoidosis, as we know it today, is an excellent example of the association of cutaneous and internal lesions. Such astute observers as Kaposi, Hutchinson, and Boeck recognized the morphologic lesions which became known as cutaneous sarcoid, and microscopic study aligned the disease with tuberculosis because of the tuberculoid structure found. The story of sarcoidosis is a fascinating one. It has taken 50 years to accumulate the known facts, and the origin is still in doubt. Dermatologists must be given the credit for recognizing the cutaneous lesions, and a brief review of the way in which, piece by piece, the syndrome as known today has been assembled emphasizes this relationship of external and internal lesions.

Sarcoidosis involves a number of tissues; in fact, the statistics on involvement reported by various observers are impressive, for in the dissemination of the disease may lie in part its comparative benignity. The reports indicate that patients with multiple foci of tuberculosis have a better prognosis. This is especially true when the skin is involved, for the skin seems to have an immunizing power; other extrapulmonary lesions also may influence each other favorably. Since sarcoidosis affects about the same tissues as tuberculosis, the resistance developed may rest on responses in a variety of tissues. The tissues most often diseased in sarcoidosis are the lungs, hilar nodes, and superficial lymph nodes, with an incidence of from 70 to 80%, while the skin, eyes, and bones show between 30 and 40% involvement. Recent studies reveal that the liver is the seat of sarcoidosis in a surprisingly high percentage of cases, but, because of the difficulties of demonstration, the accumulated cases must be regarded as representing a small proportion of the actual incidence, which, in fact, may be as high as 90% of all cases.

It is clear, however, that a disease first described by dermatologists has now been shown to be one in which the importance of the internal findings far outreaches the significance of its cutaneous identification. The variety of skin lesions which are manifestations of sarcoidosis has increased to such an extent that no longer is there an identifying lesion. Erythrodermic, lichenoid, papular, nodular, and tumorous lesions may all have the histologic character of sarcoid; we may no longer speak of specific types of cutaneous sarcoid, for the gross morphologic variations have been brought into unity by their histologic pattern.

The presence of accumulations of sarcoid tissue in various organs has not only altered function but has also brought about biochemic and physiologic changes so that bone marrow, blood, and serum may all show significant changes. The immunology of sarcoidosis has stimulated studies on tuberculin anergy. The specific test as elaborated by Kveim has eliminated to some extent the theory of a multiple origin. Dermatologists drew the attention of pathologists to the histology of sarcoidosis, and the pathologists broadened our concept of the sarcoid reaction, and as a result minute differences were shown to be of no great significance, and it is no longer proper to speak of the pathognomonic histology of sarcoidosis.

Patients with sarcoidosis have been treated with steroids, and, although the results are not uniform, the marked improvement in some patients and the remarkable disappearance of the sarcoidal inflammation suggest the need for study of the biochemic nature of the infiltrate in sarcoidosis. Such studies may elucidate the origin of this complex disease. The improvement of the patients who did respond to the administration of steroids is another observation which causes one to doubt a tuberculous origin. Here, indeed, is a disease in which the accumulated evidence as given by a number of experts is necessary in order to evaluate the condition properly.

No morphologic lesion has intrigued those interested in pathogenesis more than nodose erythema. For years dermatologists were satisfied with their view that erythema nodosum was akin to erythema multiforme. They agreed that the disease was easily diagnosed and of short course, and, because salicylates seemed to be beneficial to it, it was included with the so-called rheumatoid affections. It was known to be more severe than erythema multiforme and to have a predilection for females. Lesions which, morphologically, were more or less identical had been observed in the course of syphilis, gonorrhea, and following the ingestion of bromides and iodides, but the mechanism of the provocation was unknown. An idiopathic and a symptomatic type of erythema nodosum were postulated, and this was of some temporary benefit to the furtherance of our knowledge of the pathogenesis of the disease, if it only served to make inquiry for the possible cause a requisite.

Further doubt concerning its origin was introduced when, largely through the investigations of a number of Scandinavians, tuberculosis was incriminated as the instigator of attacks of erythema nodosum. The work of these investigators was with children, and a view was advanced and has now become well established that in childhood erythema nodosum may be a part of the syndrome of an initial tuberculous infection. Clinical observations had proved that fever, nodose erythema, and hilar enlargement were commonly associated with development of a positive tuberculin reaction and constituted a type of primary tuberculosis. Demonstration of tubercle bacilli (which could be done in gastric lavage in a fraction of the patients), when there was marked cutaneous reaction, proved the presence of active tuberculosis at the time that erythema nodosum was visible, but was this sufficient to conclude that the erythema nodosum was due to the tubercle bacillus? Bacilli have not been found in biopsy specimens in such cases, nor is the tissue reaction like that of any other form of tuberculosis. Therefore, the lesions did not appear to be the result of direct action against the bacillus, and, furthermore, the histologic findings in this symptomatic type were the same as those of the so-called idiopathic form.

The problem was somewhat clarified at the time that sulfathiazole came into use. Nodose lesions of the lower legs were often observed when the drug was administered for a variety of acute infections, and their histology conformed to the pattern that had been accepted for erythema nodosum. It was then concluded that erythema nodosum was in itself a specific reaction but that, since it accompanied certain infections or followed the ingestion of some drugs, the mechanism was one of provocation, similar to the development of herpes simplex in therapeutic malaria.

A tremendous literature has accumulated concerning the production of erythema nodosum. A great deal of it was written by authors other than dermatologists, and I am often impressed with a certain condescension to the dermatologic viewpoint, as though we had merely diagnosed the condition while others not only diagnosed it but demonstrated its cause. As a matter of fact, to date erythema nodosum can be diagnosed only as such, and, even when it accompanies or is associated with another disease, it has in most cases nothing to do with the accused basic disease. Erythema nodosum may well not be a specific disease any more than is urticaria, but its accurate differentiation from somewhat similar blotchy erythemas is one of our important tasks, while an awareness of its association with tuberculosis, particularly in childhood, is imperative.

For the sake of classification and further investigation, we may safely speak of an idiopathic, a symptomatic, and a tuberculous type of erythema nodosum, but we must not forget that morphologically and histologically the lesions are identical. Whether the production of such lesions is due to a specific cause brought into pathogenic action by a provoking drug or disease, or whether it is a type of allergic manifestation which is part of the defense of the body against an invader has not been proved. The importance placed on erythema nodosum is entirely due to its frequent and unaccountable presence during the period of establishment of a tuberculous infection, and that is reason enough to investigate every case of erythema nodosum for an important related disease. Thus a morphologic lesion may point to a more important disease. A comparison might be made with adult acanthosis nigricans, in which a lesion, to the initiated, calls for search for internal cancer. Since erythema nodosum has been found as an accompaniment of tuberculosis, sarcoidosis, coccidioidal granulomatosis, lymphopathea venereum, periarteritis nodosa, and a few other conditions, it has become a signal or warning sign and has therefore assumed a unique importance.

Lupus erythematosus is another condition the history of which is that of identification by dermatologists and gradual addition of knowledge from many sources to evolve our present concept. If chronic and acute lupus erythematosus are extremes of the same disease, then this disease is indeed unique, for such variation is not duplicated by any other.

I shall not review the history of the subject, but it is interesting to point out that the early studies were concerned largely wih the description and cutaneous pathology of chronic lupus erythematosus, while those of recent years deal with the acute and systemic forms. In the latter forms the association of cutaneous and serous membrane lesions is striking, although difficult to interpret on a histologic basis. Nevertheless, a better understanding of the general pathology of the disease has resulted, and more recently studies concerned with the phagocytic phenomenon of Hargraves have thrown some light on the immunology of the systemic type. Such studies have, I believe, separated the two major forms, for the so-called "L. E." cell (which should really be called the cell of acute and systemic lupus erythematosus) has been found even in tissues and other body fluids besides the blood and marrow in the acute and systemic condition, while its complete absence in chronic lupus erythematosus tends to separate the chronic discoid from the other forms. In fact, one might propose a classification based on the Hargraves phenomenon and speak of Hargraves-positive and Hargraves-negative lupus erythematosus, since it is

almost impossible to draw a sharp line between some cases of the so-called subacute and the acute form except on the basis of this diagnostic test.

A symposium on lupus erythematosus was held recently at the University of Minnesota, and following discussions by Klemperer, Hargraves, and others it became apparent that a new and more conclusive classification of lupus erythematosus is a necessity in order to convey the breadth of the dimensions of this disease.

A division based only on the chronicity or acuity is inadequate, because Hargraves and Haserick's investigations have shown conclusively that results of their tests may be positive in critically ill patients whose condition has lasted for months or even years, although many such patients did not at any time have cutaneous lesions. These cases constitute a group to which the term protracted systemic lupus erythematosus might be applied. In studying patients who belong to this group, it was discovered that they usually had a history of a slow, insidious addition of symptoms which finally added up to the presenting status at collapse, and that the complaint at that time could be very misleading. The Hargraves and Haserick tests, therefore, have become a necessity in the diagnostic approach to patients with a history of unexplained symptoms of decline, fatigue, loss of weight, diarrhea, periods of fever, etc. I shall not describe in detail the clinical picture of the condition which, for the want of a better name, I am calling protracted systemic lupus erythematosus. I believe it is imperative that this condition be recognized as a severe, often fatal, form of lupus erythematosus which, in addition to the acute septic form of lupus erthematosus constitutes a frequent and at present unexplored type of the disease. If one accepts this group, and I do, as part of lupus erythematosus in its broad sense, one realizes how far we have come from the early descriptions of chronic and acute lupus erythematosus.

Thus, lupus erythematosus, erythema nodosum, and sarcoidosis, all diseases which historically were dermatologic conditions, have, with the advances in diagnosis, become important entities which are the concern of all diagnosticians, and our position in relation to these diseases depends entirely upon our keeping abreast of all additions to the inclusive present-day concepts. The question is not to which specialty such diseases are assigned; it is a matter of the total knowledge which can be accumulated and applied for the patient's benefit.

Despite the ingenuity of many investigators, the origin of lupus erythematosus remains unexplained. Tuberculosis, streptogenic disease, a form of rheumatic disease, these and other hypotheses have been advanced, but no conclusion was permissible on the evidence produced. The studies of Klemperer have shown beyond a doubt that the pathology of systemic lupus erythematosus is very widely disseminated and fairly uniform in all tissues involved, but to the present the pathology has not given a clue to the origin. It is hoped that the discovery of the cause is imminent.

Trial of therapeutic agents whose efficacy was proved in other diseases has to some extent furthered our knowledge. For example, calciferol has no effect on the chronic form of lupus erythematosus. The sulfonamides and the antibiotics have had some effect, even at times striking results, on the acute form. Penicillin has been reported by some to be effective during a febrile period in that form of lupus erythematosus which is disseminated but is accompanied with minimal systemic symptoms. Because of the factor of light sensitivity and a pellagroid distribution in

lupus erythematosus, vitamin B complex and some other vitamins have been used, and in the chronic form some favorable results have been noted. Results of the use of the steroids in acute lupus erythematosus are still in a controversial stage, but the striking amelioration of symptoms may have some significance, if only to align the disease with others that respond to administration of the steroids. Both gold salts and the steroids have been used with various degrees of success in arthritis as well as in lupus erythematosus. Does that fact relate these two rather inclusive conditions?

In listing the types of lupus erythematosus that I believe should be recognized at present, I do so not in order to propose a classification but rather in the hope that, in our teaching, students may acquire a broader concept of the disease and a realization that an almost imperceptible facial erythema may be the forerunner or first recognizable symptom of a very severe disease.

TYPES OF LUPUS ERYTHEMATOSUS

1. *Acute Localized Edematous Type.*—(This form is often omitted in classification.) The lesions appear as erythematous, sharply circumscribed disks which feel like an elastic node. In a short time the node shrinks, leaving a superficial red spot having a central depression. The lesions may disappear without a trace or become transformed into the ordinary discoid variety.

2. *Chronic Discoid Type.*—These lesions may vary as to size, number, and morphology.

3. *Chronic Disseminated Type.*—The lesions may be large and extensive in distribution, and when they occur over large body areas the condition is called the psoriatic type of chronic lupus erythematosus, a rare form. Systemic symptoms are not striking, and results of the Hargraves and Haserick tests are negative.

4. *Subacute Disseminated Type.*—This type includes conditions in which activity of an exudative nature may be noted in the individual lesions, accompanied with mild systemic symptoms, as well as those in which the lesions are widely distributed, of a toxic-erythema or erythema-multiforme-like character, and are accompanied with noteworthy but not severe systemic symptoms. Results of the Hargraves and Haserick tests may be either negative or positive, depending upon the severity of the condition. These cases always may become acute and must be handled accordingly.

5. *Acute Disseminated Systemic and Septic Type.*—Acute disseminated lupus erythematosus with cutaneous and mucous membrane lesions, accompanied with high septic temperatures and other well-known findings, is an acknowledged dermatologic entity. Results of Hargraves and Haserick tests are positive, and patients are in immediate danger of death. Fortunately, the newer therapy with the steroids offers some hope for improvement and even recovery.

6. *Protracted Systemic Type.*—Patients with the protracted systemic type of lupus erythematosus have a long, indefinite history of general decline. The cardinal symptoms of fever, arthralgia, loss of weight, etc., and the blood changes, albuminuria, and hematuria of the septic type of the disease must be carefully sought, but the presenting symptoms may be very misleading. The Hargraves and Haserick tests yield positive results and are the only means of definitely identifying the syndrome. Occasionally there are patients for whom results of the test are negative initially and become positive only with continued decline and fever. Therefore,

patients whose symptoms place them in this category and whose reactions are negative should be observed, and the tests should be repeated a number of times. Provocation of a positive reaction may be brought about by an intercurrent infection, and possibly an artificial means may be advocated, such as inducing fever.

Review of the accumulated knowledge about lupus erythematosus, its phases, its transformation of type, or its behavior under therapy leaves much to be desired and impresses one with the need of cooperative studies. We, as dermatologists, have the opportunity to make more thorough systemic studies of the chronic form. Revealing facts concerning its relationship to the vascular system and to hormonal influences may be found which would assist materially in solving the entire problem of lupus erythematosus.

Dermatologists have diagnosed and treated cutaneous cancer from the earliest days of the specialty and have contributed considerably to the knowledge concerning the so-called precancerous lesions and the external carcinogenic substances, but studies on endogenous influences have been neglected. Granting the existence of precancerous lesions which may prepare the tissues for cancer, what is the continuing cause which maintains cancer cells and stimulates them to produce their kind and protract their growth? Dermatologic research should be in a position to assist in such a problem. Advances have been made in the knowledge of cancer of the sexual organs, as evidenced by the results of hormone treatment of prostatic cancer. In such cancers, age at occurrence and the failing of hormone equilibrium coincide, and consequently an endogenous cancerogenic substance or influence may be sought by investigating the endocrine glands concerned.

Cutaneous cancer also is found in the climacteric years. Surely external influences alone cannot account for cutaneous cancer occurring in the last third of life expectancy. Furthermore, it is impossible to state that every skin cancer begins with a predisposing lesion, for many such cancers begin insidiously as miniatures of the larger cancerous lesion. Even if one admits a definite and genuine precancerous lesion, such a lesion does not account for the continuation of new growth once it has started. In fact, here again the time element, i. e., the aging of the host, becomes important. This is exemplified in the x-ray dermatitis of physicians' hands. They often have severely damaged skins, but only when they reach older age do frank epitheliomas develop frequently and rapidly.

The histology of cutaneous cancer has been of tremendous value in differentiating types, in classifying, and in prognosis, but there is much to be desired in interpretation of the histologic findings. Microscopically, basal-cell cancers are hard to understand, both as to cellular origin and because of their great variety of structure. If basal-cell cancers originate from the basal layer and retain their embryonic type without differentiation, a more uniform general topography would be expected. On the contrary, solid masses or dainty lace-like filaments are found which remain attached but penetrate deeply into the cutis, and even when the cell structure is generally uniform, here and there in a microscopic section various adenoma-like arrangements may be found, and even cornification, which confuses the diagnosis. However, the interpretation of the histologic structure of the neoplasm is the first step; far beyond it may lie those unknown factors that determine which cells shall be influenced and in what way.

I have mentioned only a very few conditions in which boundaries between dermatology and other branches of medicine cannot be drawn. There are many,

many more; in fact, it is nearly impossible to point out a disease that is strictly cutaneous.

Dermatopathology continues to be one of our most valuable aids in studying skin diseases, even though humoral and cellular pathology are pretty well united in our present approach to pathogenesis of cutaneous diseases, wherein speculation or intuitive deduction may be indulged in but the accuracy of microscopic diagnoses is still respected; and, with the application of new staining methods and chemical microscopy, the study of histology will continue to add to our knowledge of pathologic processes.

One need only mention diseases of the hematopoietic system to appreciate the impossibility of diagnosing neoplastic infiltrates without the expert aid of one versed in precise cytology. The great advances in hematology have been a boon to dermatology, not only in diagnosis but more broadly in opening a field for investigation of such poorly understood diseases as, for example, urticaria pigmentosa and lupus erythematosus, in which much information has been gained.

There are many new methods of investigation which should be applied to dermatology. In recent years the study of blood plasma has been greatly improved by the introduction of new methods, such as electrophoresis, the use of ultracentrifuge, alcohol fractionation, and others. Dysproteinemia as originally defined was interpreted as a disproportion between different kinds of normal proteins of the blood plasma, while paraproteinemia denoted the appearance of proteins normally not found in the blood. Diseases such as urticaria, the prurigos, certain eczemas, amyloidosis, pemphigus, and the purpuras offer a fertile field for investigation by means of blood-plasma studies. Such research might not only reveal etiologic factors but even suggest therapeutic procedures for diseases which are now intractable.

One of the problems now confronting dermatologists, as I see it, is to interpret our diagnoses. Our efforts accurately to describe and label cutaneous manifestations have been laudable. We, as specialists, have become proficient in recognizing and classifying the many conditions with which we deal, but too often we are unable to explain the significance of our diagnoses. From those cutaneous conditions definitely associated with well-understood systemic conditions, it is possible to draw conclusions that may point out lines of investigations to be made on skin diseases the morphologic lesions of which are clinically and histologically similar to those known to occur in such association.

The need for the most intimate association of dermatology with general medicine is obvious. Nearly every new diagnostic and therapeutic procedure in medicine is applicable to certain skin diseases. In utilizing the special skills and new knowledge from all fields of medicine, dermatology will advance, and its advances will, in turn, contribute to the unified and constant effort of medicine to learn the causes and effects, that is, the natural history, of diseases.

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ABSTRACT OF DISCUSSION

DR. OSCAR GANS, Frankfurt, Germany: With a masterly hand my friend, Henry Michelson, has painted a picture of present-day dermatology, which allows one to view the slowly developing trend of German dermatology in the past 20 years. During that time dermatologic research in Europe, particularly Central Europe, has developed in two directions. In the one, it has explored

the possibilities of new therapeutic discoveries, and in the other direction, the application of pathological physiology. During this time morphologic and histopathologic research has been pushed more and more aside.

Now, since Hebra and Unna, morphology has been considered the basis of dermatology, and as I have stated in a paper before, dermatology must remain morphologic, or there will be no dermatology.

The history of modern dermatology is based on the clinical fundamentals which Hebra erected 100 years ago and on the histologic structure which Unna provided by his endeavors "to see clinically with an eye trained by histology and mi. oscopically with an eye trained by dermatology."

I must admit that the tremendous amount of detailed morphologic facts which have been collected all over the world in the last century is a heavy dose for the younger generation to digest. It is much easier and quicker to quote startling discoveries and to apply new methods than it is to learn dermatology in the old way. Research workers are assured that they may find new facts without mastering the old, but to me that is like a ship without ballast, for a research worker cannot sail a steady course unless he has the stabilizing influence of mastery of morphology.

I should very much hate to see dermatology lose this morphologic basis, and I think that, if it were to be lost and research were to replace it, dermatology would be washed back into general medicine.

PREGNANCY AND APOCRINE GLAND DISEASES: HIDRADENITIS, FOX-FORDYCE DISEASE

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USEFUL literature on pregnancy and its effects on the skin and cutaneous diseases is scattered and for the most part sketchy. The clinician would lose little by confining himself to about three good, modern reviews, if he did not care to exhaust the subject of this relationship. Latterly there has been an increasing number of studies on the influence of pregnancy on both the physiology and the pathology of the skin. It is to be hoped that all this work of a fundamental nature will in the end prove of benefit to us in clinical dermatology.

As the reader mulls over the several worth-while reviews, he is immediately struck by the disagreements and divergent opinions they contain. Here and there he finds an attempt to strengthen with statistics the validity of some contention, but all of us have learned to shy away from and be suspicious of this method of proof. For the greater part, the data are inadequate, because, after all, most of us even in favorable situations see only enough material to form mere opinions.

Reviews on the subject of the influence of pregnancy on skin diseases use several forms of classification. Costello [1] lists the diseases according to their presumed causes, endocrinal, toxic, and neurogenic. Hollander and Vogel [2] group skin diseases according to whether in their opinion pregnancy precipitates, aggravates, or improves them. Crawford and Leeper [3] collected an impressive amount of statistics to bolster their opinions, and, in spite of what I said above about the difficulties besetting the statistical method, it has helped their conclusions to stick. I am sure, however, that they would be the first to admit that the subject matter remains controversial. Some good observers believe, even, that there is very little causal connection between pregnancy and any one skin disease.

It seems to me that it might be more profitable if we were less ambitious and surveyed just a small corner of this presumed relationship, a sphere where it seems fairly certain that the endocrines are basic. Hormones are important in pregnancy and also modify some of the components of the skin, one of these, the apocrine

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Presidential address before the Chicago Dermatological Society, Jan. 17, 1951.

From the Departments of Dermatology, University of Illinois College of Medicine, and the Cook County Hospital.

1. Costello, M. J.: Eruptions of Pregnancy, New York J. Med. **41**:849 (April) 1941.

2. Hollander, L., and Vogel, H. R.: Notes Concerning Some of the More Frequent Skin Diseases Occurring During Pregnancy, Pennsylvania M. J. **48**:454 (Feb.) 1945.

3. Crawford, G. M., and Leeper, R. W.: Diseases of the Skin in Pregnancy, Arch. Dermat. & Syph. **61**:753 (May) 1950.

glands, quite obviously. For this reason, it seems to me there might be an advantage in focusing our attention on the diseases of the apocrine glands to see what influence, if any, pregnancy has on them.

There has been knowledge of the apocrine glands for over 100 years, but despite this, for a long time they received little attention. Fox and Fordyce gave a masterful description of the disease that bears their names but apparently did not realize the specialized terrain of the affection. It was not until the classic studies of Schieffer-

Fig. 1.—Fox-Fordyce disease.

decker on the anatomy and function of the apocrine glands that these structures came into their own, so to speak.

The times in the life cycle when the apocrines become active, reach their zenith, and then decline makes it seemingly obvious that these glands are under the direct influence of the sex hormones. These organs appear at puberty, a time, too, when a growth of hair in connection with them is somewhat suggestive. They must have some earlier awakening than that, however, because I saw and recorded a case of Fox-Fordyce disease in a girl 9 years old, three years before she showed manifest signs of puberty. The apocrines are said to become smaller and secrete less after the menopause, but it is agreed that they enlarge and become more active just before

and during the menses. For some unknown reason, diseases of these glands appear mostly in women. While they may affect men, this must be rare, and I do not remember ever seeing it. Women have a larger number of these glands than men, and Negroes more than white persons. In keeping with this, I have seen a greater number of cases of apocrine diseases in Negro women, but this may be because of the very large number of Negroes I see at the Cook County Hospital.

There is some disagreement about what happens to the apocrines during pregnancy. Some writers have thought that these glands enlarge at this time and then

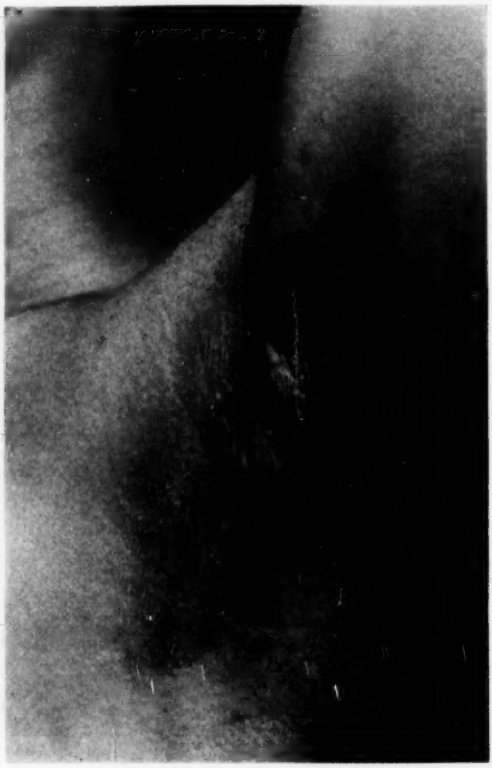

Fig. 2.—Fox-Fordyce disease (early pregnancy).

give off more secretion. More investigators, however, have found the contrary to be true, namely, that these organs are less active during gestation. I thought it would be of some merit in this controversy to see what happens to apocrine gland diseases in women becoming pregnant. Without proof we would assume, of course, that a disease affecting a gland would be less severe when that organ was less active, and vice versa.

REPORT OF CASES

1. *Fox-Fordyce Disease.*—A Negro woman, 24 years old, had had an eruption of Fox-Fordyce disease in the axillae and over the pubis for two years. She said that it came on shortly after the birth of her son and had become progressively worse. I tried a number of remedies to relieve the

severe itching only to find that they helped very little indeed. Just at the time when she was taking moderately large doses of vitamin E, she reported that the itching was abating, and we could see the eruption subsiding. A little later, all the itching ceased, and the skin at the armpits looked baggy, something like that seen in pseudoxanthoma elasticum. The improved areas had a dull purplish color and were slightly scaly. It was at about this time that I became aware that the patient was pregnant, three and one-half months, she said. Of course, it occurred to me at once that the improvement in the axillae might be due to her gravid state, so I promptly discontinued the vitamin-E therapy. In spite of this, she continued to improve without any other treatment. Her axillary hair regrew but remained sparser than that of most women, but this may have been because her eyebrows and hair growth in general were thin. The axillae continued to

Fig. 3.—Hidradenitis suppurativa (seven months pregnancy).

improve still further, but were not entirely well at the time of confinement. A month afterwards there was a partial regression, and this state prevailed until she weaned her twin daughters five months after delivery. Two weeks after this, the eruption and pruritus were back to their original intensity. At this time she had another trial with vitamin E, but without any noticeable effect. In the meantime most of her axillary hair again fell out. There is nothing noteworthy to say about all the laboratory work that was done in connection with her case. A biopsy of axillary skin showed the changes characteristic of Fox-Fordyce disease. Histologically, what impressed us most was the relative inactivity of the apocrine glands as shown by the almost uniformly flat character of their epithelium.

2. *Hidradenitis Suppurativa.*—A Negro woman, 21 years old, had been having for over three years recurring abscesses with sinus formation and puckered scarring in the axillae and about

the areola of the right breast. The condition improved at times but never to the point of giving complete relief. The lesions began to regress, pain and tenderness were ameliorated, and she could raise her arms easily when she had been pregnant for two and one-half months. This improvement continued and progressed until the time of confinement, when the axillary lesions had apparently healed completely, and there was no remaining pain or tenderness. A small discharging sinus on the areola of the right breast was the only sign of activity that remained. During all of this interval there was no regrowth of hair at the axillae. Unfortunately, the patient did not return for observation after her delivery, so we were unable to see what effect the nongravid state had on her hidradenitis.

3. *Hidradenitis.*—A white woman, 32 years old, had been having for four years recurring abscesses and draining sinuses from both axillae, the perineum, buttocks, and upper thighs. The skin was distorted by numbers of scars. All our treatments with x-rays, various hormones, local applications, and general measures helped her very little. But she was able to move her arms without pain from the time she was 3 months pregnant, and we could see that all her lesions were becoming less active and healing. Two places, however, flared up again at the time when she would have had her fourth menstrual period. Several days after this she again began to improve. The entire process in her axillae continued to decline and seemingly became entirely inactive. The axillary hair growth, however, continued to be sparse and did not thicken. She gave birth to a boy and nursed him for a month. Two months after she weaned him, both her axillae showed renewed activity but to a lesser extent than before.

COMMENT

Treatment today for Fox-Fordyce disease and hidradenitis is far from satisfactory. In some of the severe cases we must still resort to surgery and plastic repair. This is so because none of the physical or local measures has been very successful for some of us. Nor has systemic treatment, even with modern hormone products, been of any more help. Naturally, when patients show improvement during pregnancy, we look to see what changes in the endocrine balance could account for these happy results. The variations in the hormonal pattern which pregnancy brings about are known in a general way, but this information has not furnished us with a successful clue for combating the apocrine diseases. None of the available glandular products known to be increased during pregnancy was of any help to our patients when we administered them. Investigators have isolated steroid substances that make their appearance only with pregnancy. Perhaps these temporary products would be of more help for our purposes.

Way and Memmesheimer,[4] in an excellent review and study, said, ". . . during the premenstrual period and during pregnancy there are hypertrophy and hypersecretion of the glands. These findings show an obvious correlation between the apocrine glands and the sexual organs and justify the name 'accessory sexual glands.'" These authors refer to the work of Löschke[5] and Waelsch,[6] who found that the apocrine glands enlarge during menstruation. I was not certain after a careful study of their paper why they concluded that these glands are more active during pregnancy. They furnished excellent illustrations, but none that showed the appearance of these structures during the gravid state. Nor was I sure that they made other than histological studies.

4. Way, S. C., and Memmesheimer, A.: The Sudoriparous Glands: II. The Apocrine Glands, Arch. Dermat. & Syph. **38**:373 (Sept.) 1938.

5. Löschcke, H.: Über zyklische Vorgänge in den Drüsen des Achselhöhlenorgans und ihre Abhängigkeit vom Sexualzyklus des Weibes, Arch. path. Anat. **255**:283, 1925.

6. Waelsch, L.; Kayser, F., and Seitz, L.: Cited by Way and Memmesheimer.[4]

On the other hand, Richter [7] was of the opposite opinion regarding the activity of the apocrines during pregnancy. He made an exhaustive study of the normal and pathologic anatomy of these glands and said that they show a decline and that their secretions lessen during pregnancy. Pinkus,[8] also, thought that the activity of these structures is reduced during the gravid state. To me too it seems that these glands are seen in their resting stages more often in tissue removed during pregnancy. I counted 50 acini in skin sections taken from a pregnant woman and compared their activity with an equal number counted in tissue taken from a nonpregnant one. Both subjects were comparable, being Negroes and in their twenties. Thirty-three of 50 acini in the tissue from the nonpregnant woman were in an active phase; whereas, in the skin of the pregnant woman only 16 out of 50 were active. Whatever trust we may put in this overly simple approach, it would seem to suggest that the apocrines are less active during pregnancy. For more convincing evidence we need methods that are able to measure the amount and composition of apocrine sweat secretion.

These glands are said to contain large amounts of iron, cholesterol, and fat. Possibly histochemical methods visualizing these three materials might give us indirect evidence of the comparative activity of the apocrines during pregnancy and in the nongravid state. Pregnancy seems to affect the acini in two ways: (1) by lengthening the inactive span of their cycles or, put another way, by shortening their active phase, and (2) by preventing entire glands or parts of glands from acting at all. From morphologic appearances alone, either one or both of these hypotheses could be true.

Pautrier took part in a discussion of a case presented by Gougerot and Blum.[9] He said that he observed a woman who had Fox-Fordyce disease and severe itching until she interrupted her visits to his clinic. She resumed the visits when her itching and eruption recurred after the delivery of her baby. In the interval of her pregnancy she had become entirely free of her pruritus, and at the same time her skin lesions disappeared.

Netherton [10] described the case history of a woman with Fox-Fordyce disease who also had hyperthyroidism. After her thyroid was removed, her itching disappeared almost entirely, and with that the eruption, too, became inconspicuous. On unusually busy days she had recurrences of a little pruritus. Why such a sequence of events appeared in this case is not clear in the light of our experience. It is well known that pregnancy increases the activity of the thyroid and should on that account make Fox-Fordyce disease worse, if that gland were decisive in this disorder. We made no observations on the thyroid activity of our patient, but if it was increased, as it probably was, we believe it acted merely as an incident to the clinical course of the skin disease. It seems more likely to us that the reshuffling of the checks and balances of the steroid hormones that comes with pregnancy will be

7. Richter, W.: Contribution to Normal and Pathologic Anatomy of the Human Apocrine Glands, Arch. Path. Anat. **287**:277, 1933.

8. Pinkus, F.: The Normal Anatomy of the Skin, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, Vol. 1, pp. 1-369.

9. Gougerot, H., and Blum, P.: Fox-Fordyce Disease Without Pruritus, Bull. Soc. franç. dermat. et syph. **39**:700, 1932.

10. Netherton, E. W.: Fox-Fordyce Disease Associated with Hyperthyroidism, Arch. Dermat. & Syph. **13**:794 (June) 1926.

found in the end to account for the condition which we saw at the clinical surface. This opinion does not deny in any way the role of an augmented metabolic activity in making a patient more irritable and in that way intensifying the itching.

Most apocrine ducts empty through follicles, so that it is small wonder that diseases involving the glands should affect the adjacent hair growth too. In Fox-Fordyce disease the hair at affected sites becomes stunted or disappears entirely, while in hidradenitis a patch of alopecia makes its appearance over the entire surface of an abscess. Hair growth in hidradenitis behaves very much as it does in periadenitis capitis abscedens et suffodiens. It is curious that hair should fall from expanded areas even before their follicles can be shown morphologically to be involved.

It is noteworthy, too, that the diminished hair growth accompanying Fox-Fordyce disease is reversible, as was shown by the way the axillary hair regrew in our patient during her improvement. Some believe that the hair loss that occurs is due to the rubbing and scratching incident to this chronic and rebelliously itching disease. Supporting this view is the commonplace observation of the loss of hair that follows the trauma of scratching or the pressure of a garter or brace. Yet the chronic hyperkeratosis and plugging of follicles, together with other more subtle changes, appeal to me as causes of hair loss more than those gross mechanical factors. In contrast to what occurs in Fox-Fordyce disease, the hair loss in hidradenitis is irreversible. Neither of our patients regrew hair during her improvement. The same is true of periadenitis capitis abscedens et suffodiens: The hair does not regrow when the disease burns itself out.

Curtis [11] presented the case of a woman who, besides having hidradenitis, showed the changes of pituitary basophilism (Cushing's syndrome). He was of the opinion that the two diseases did not exist side-by-side coincidentally, but rather that both had a common denominator, probably, in the increased quantity of androgens made available by the adrenal cortex.

We naturally turn to the estrogens and progesterone as likely explanations of the pathogenesis or even as possible therapeutic agents for the relief of the apocrine diseases. Pick [12] claimed that he gave his patient with Fox-Fordyce disease relief by using ovarian and corpus-luteum extracts. Unfortunately, I was unable to corroborate his favorable results when I employed our more modern estrogenic preparations and progesterone. The curve of the intrinsic availability of these products during the entire period of pregnancy is well established and characteristic. The clinical course of events in our patients as we watched them did not run exactly parallel to this curve. Hence, I am inclined to believe that the estrogens and progesterone are not of great moment in either the production or amelioration of the apocrine diseases, even though these maladies occur characteristically in the female. The observation of Hench and Kendall that rheumatoid arthritis is often improved during pregnancy furnished them with an important clue that led to the elaboration of cortisone and corticotrophin (ACTH) with such epochal results. Because our patients with apocrine diseases, too, improved during their periods of pregnancy,

11. Curtis, A. C.: Cushing's Syndrome and Hidradenitis Suppurativa, Arch. Dermat. & Syph. **62**:329 (Aug.) 1950.

12. Pick, W.: Pathogenesis of Fox-Fordyce Disease, Arch. Dermat. & Syph. **13**:478 (June) 1926.

we perhaps ought to be tempted to employ these new hormones for their relief. In view, however, of Curtis' clear-cut case report of associated hidradenitis and pituitary basophilism, it is doubtful if these products which are known to be capable of inducing the one could be of help to the other.

SUMMARY

Cases are presented of one woman with Fox-Fordyce disease and two with hidradenitis suppurativa who had remissions or were greatly improved during their periods of pregnancy. The disease in two of them relapsed after their delivery. The third patient disappeared from our view after she came to term. There is a discussion of the relationship existing between the apocrine glands and diseases and some of the endocrine glands and products. It appears from other peoples' work and ours that the apocrine glands are found in a resting state more often and secrete less during pregnancy than when the subject is in the nongravid state. This dampening effect of pregnancy on their functional activity may be the key to explanation of the amelioration of apocrine gland diseases during the gravid state.

1819 W. Polk St.

DERMATOLOGY IN EGYPT

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AS EARLY as the Ancient Egyptian Empire, about 3500 B.C., medical men were held in high esteem in Egypt. During the reign of King Josher of the 3d Dynasty (2700 B.C.), Imhotep, a man who had distinguished himself as an architect and physician, was divinified posthumously as the son of Sekhmet, the Goddess of Medicine.[1]

Hieroglyphic inscriptions and engravings indicate that many of the diseases from which the Ancient Egyptians suffered are those which still afflict their descendants. Among the diseases mentioned are leg ulcers, the "Nile boil," hematuria (probably bilharziasis), and leprosy. Elephantiasis of the lower extremities can be recognized in the statue of Pharoh Menthuhotp (2000 B.C.). The swelling involves both feet and the legs to just above his knees.[2]

Archeologists have found fairly definite remnants of the existence of tuberculosis, evidenced by Pott's disease in the spine of a priest of the 21st Dynasty (2500 to 1500 B.C.). No traces of syphilis have been demonstrated;[1c] this has been interpreted as corroborative evidence by those who theorize that the disease was introduced from the Western Hemisphere following Columbus' expedition.

Ancient Egyptian medical men are known to have prescribed medicine in ointments and poultices for local application. Fat was the vehicle for ointments.[1c]

The foundations of modern medical education in Egypt were laid with the establishment of Kasr El-Ainy Hospital and Faculty of Medicine in Cairo. Madden has given a comprehensive description of the history of this School of Medicine.[4] Kasr El-Ainy was built in 1466 as a palace where distinguished visitors were

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1. (*a*) Wright, A., and Cartwright, H. A.: Twentieth Century Impressions of Egypt, London, Lloyd's Greater Britain Publishing Company, Ltd., 1909. (*b*) Sobhy, G.: Lectures in the History of Medicine, Cairo, Fouad I University Press, 1949; (*c*) A Short Account of Ancient Egyptian Medicine, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 2, Cairo, Imprimerie Nationale, 1929. (*d*) Garry, T. G.: Imhotep, the Reputed First Physician and Egyptian God of Medicine, ibid., Vol. 2, 1929.

2. Kamal, H.: Methods of Diagnosing Diseases by the Ancient Egyptians, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Cairo, Imprimerie Nationale, 1929.

3. Footnote deleted.

4. Madden, F. C.: Thirty Years of Surgery in Kasr El-Ainy Hospital, 1898-1928, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 3, Cairo, Imprimerie Nationale, 1931.

entertained, and it was for a time the residence of the Turkish viceroys. During Napoleon's occupation (1798) it was used as a hospital. With the departure of the French Army (1801), it ceased to be a hospital until 1837, when it was reopened by Clot Bey, the Surgeon-in-Chief of the Army of the famous Mohammed Aly Pacha, first khedive of Egypt.

From 1837 to 1849 professors were imported from the French schools of medicine. In 1849 the faculty became predominantly German; it included such distinguished names as Griesinger, Royer, and Bilharz. Bilharz described Schistosomia haematobium, the causative agent of bilharziasis (schistosomiasis), from autopsy studies at Kasr El-Ainy Hospital. Following the Germans, there was a brief period of Italian control (1854). In 1863 the first native Egyptian was appointed director, and the school continued under local administration until the British occupation of Egypt (1882).

In 1884 Herbert Milton became director of Kasr El-Ainy. It was during his tenure that modern methods of surgery and asepsis were introduced. Under Milton's administration the hospital grew to tremendous size and importance. It became renowned throughout Egypt and attracted thousands of patients, many of whom came from great distances.

The Department of Dermatology was organized in the School of Medicine in 1898, during the extensive reorganization of the faculty as part of the Fouad I University. The first chief of dermatology was an Egyptian physician, Aly Bey Haider.[4]

Today Kasr El-Ainy Hospital is one of the largest in the world. It has a capacity of about 3,000 beds and a tremendous outpatient clinic service. The hospital is a public institution under the administration of the Ministry of Health. The faculty of the School of Medicine of Fouad I University, which uses its facilities for clinical teaching and research, is under the Ministry of Education.

Kasr El-Ainy was the only medical school in Egypt until 1943. In that year a second faculty was inaugurated as part of Farouk I University in Alexandria, and in 1946 a third was opened in the Demerdash Hospital in Cairo. The three schools together graduate about 300 physicians each year.

The prerequisites for admission to a Faculty of Medicine include a primary school certificate (four years), a secondary school certificate which represents five years' study, and one year of successful study in the Faculty of Sciences as evidenced by passing the Preliminary Natural Sciences Examination. The medical curriculum is designed to take a period of five and one-half years and is patterned from the British schools. To graduate, the student must pass an examination for the degrees of Bachelor of Medicine and Bachelor of Surgery, which are the equivalent of the same degrees in England. The examinations are supervised by the Royal Colleges of Surgeons and Physicians of England.

Undergraduate teaching in dermatology and venereology consists of didactic lectures and clinical instruction (outpatient and ward) in grouped sections occupying a period of 12 weeks in the medical curriculum.

Formalized postgraduate programs in the various specialties were begun in 1939 at the Kasr El-Ainy Hospital. The prescribed course in dermatology and venereal diseases takes 12 months, in addition to the required year of internship. The postgraduate curriculum includes the study of dermatopathology, bacteriology, mycology, x-ray therapy, and clinical dermatology. On completion of this year, the physician-student is given a written examination by the senior members of the departmental

staff. If he passes this, he is admitted to an oral examination in each of the subjects studied. Successful candidates are given certificates of specialization in dermatology and venereal diseases by the Fouad I University.

There are over 4,000 practicing physicians in Egypt, 114 of whom specialize in dermatology and venereal disease.

The Ministry of Health plays an important role in the medical-care program as well as the public health of Egypt, since patients who can afford private care are in the minority.

There is a Skin and Venereal Disease Section in the Ministry of Health. Since its inception 25 years ago, when it had two lock-hospitals for the treatment of prostitutes and four outpatient skin and venereal disease clinics, the Section has grown to 47 clinics, of which 3 have facilities for inpatient care. The lock-hospitals, as such, were closed in 1948 with the abolition of prostitution. The Section employs 56 physicians, many of whom have had specialized training in European centers or at

*Incidence of Skin Diseases in Egypt (Port Said)**

Disease	No. Cases		Percentage	
1. Impetigo and pyogenic infections		5,220		32.7
a. Impetigo	3,882		24.3	
b. Sycosis	98		0.6	
c. Other pyogenic conditions (boils, carbuncles, furuncles, hydradenitis, etc.)	1,240		7.8	
2. Scabies		4,125		25.8
3. Mycotic infections		2,082		13.0
a. Tinea capitis	590		3.7	
b. Favus	42		0.3	
c. Tinea pedis	930		5.9	
d. Other types	514		3.2	
4. Eczema and dermatitis		2,589		16.2
a. Eczematous-contact-type dermatitis	1,701		10.7	
b. Atopic eczema	296		1.8	
c. Urticaria	592		3.7	
5. Syphilis (all types)		745		4.7
6. Acne vulgaris		389		2.4
7. All other diagnoses		830		5.2
Total		15,980		100.0

* Tabulated from the records of the Port Said Clinic, 1946-1948.

the Kasr El-Ainy Hospital. With the exception of the director and two assistant directors, the physicians are part-time employees. They usually devote each morning, except Friday (the Moslem Sabbath), to their clinics and afternoons to private practice.

In 1943 the Egyptian Association for the Study of Skin and Venereal Diseases was organized. Dr. Gamal El-Din El-Hefny Bey, Director of the Section of Skin and Venereal Diseases of the Ministry of Health at that time, was the primary instigator. The Association holds official meetings semimonthly, usually in Cairo. Programs consist of case presentations and discussions, and reading of scientific papers. The *Journal of the Royal Egyptian Medical Association* is now the Association's official organ, but it is hoped that a specialty journal will be possible in the near future. There are 57 physician members in the Association.

In order to present a picture of the type of dermatologic material encountered in Egypt, we have tabulated the incidence of the most common diagnoses based upon 15,980 patients' visits to the Port Said Clinic for Skin and Venereal Diseases from 1946 through 1948. Port Said is a city of approximately 150,000 inhabitants, located at the northern entrance to the Suez Canal. It cannot be considered a strictly urban

community, but rather a mixture of urban and rural. There are two Ministry of Health clinics devoted to dermatology and venereal diseases; each operates six days weekly from 8 a. m. to 1 p. m.

SCABIES

Scabies is the skin disease seen most commonly in dermatologic clinic practice in Egypt. Animal scabies is fairly common; the usual sources are camels, cats, and cattle. It is easily differentiated clinically from human scabies by the patient's history, the absence of burrows, and the localization of the lesions (maculopapular and papulopustular) to certain areas of the body, depending upon the mode of contact with the source. Quite often, however, a generalized eruption occurs. The response to treatment with benzyl benzoate preparations is equally good in animal and human scabies.

IMPETIGO AND OTHER PYOGENIC DERMATOSES

Impetigo is an extremely common infection. All types are seen, but there is a relatively high incidence of the bullous type in children.

In the early spring and late summer, furunculoses and large carbuncles are frequently seen. The lesions often occur in groups and appear on many parts of the body, but particularly about the face, scalp, and buttocks. Although this condition is observed in persons of all ages, it is most common in small children. Carbuncles of extremely large proportions are referred to as "Nile boils." The responsible organism is the Staphylococcus (Micrococcus) pyogenes aureus. Individual lesions can often be aborted within 48 hours by the injection of penicillin in aqueous solution into and around the lesions. A course of Staphylococcus vaccine injections seems to be effective in preventing recurrences.

During the humid summer months, miliaria rubra (prickly heat) is quite common. It is popularly called "Nile heat" because the river Nile reaches its highest levels during this time of the year. Secondary pyodermas are seen in patients with miliaria rubra.

MYCOTIC SKIN DISEASES

Superficial Mycoses.—Many clinical types of superficial fungous infections are encountered in practice. These include dermatophytosis, onychomycosis, tinea corporis, tinea capitis, favus, tinea circinata, cutaneous moniliasis, tinea versicolor, tinea barbae, and erythrasma. Lepothrix, piedra, parasitic achromia (hodi-potsy), tinea imbricata (Tokelau), and chromoblastomycosis have been recorded,[5] but are not frequently seen.

There are no statistical data on the relative frequency of the species of fungi responsible for tinea capitis in Egypt. Trichophyton violecaum, T. crateriforme, T. acuminatum, and T. gypseum have been isolated by culture on Sabouraud's medium from infected hairs of school children.[6] A study of the children seen in the Port Said Clinic indicated a higher incidence of Tricophyton than Microsporum infections. Microsporum lanosum is more common than M. audouini.

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5. Gohar, N.: Mycoses and Practical Mycology, ed. 1, London, Baillière, Tindall & Cox, 1948.

6. Scander, N.: Fungus Diseases of the Hair in Egypt, Compte Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 3, Cairo, Imprimerie Nationale, 1931.

In 1943 Hammouda and Mikhail administered thallium acetate to 60 orphanage children with tinea capitas. The dosage was 8.5 mg. per kilogram of body weight; all were treated at the same time. No toxic reactions were observed. Epilation occurred between the 14th and 17th day. An ointment of 5% sulfur and 5% salicylic acid was used locally. All were cured. Excellent results have been obtained in an additional 40 patients treated at the Port Said Clinic.

Favus (due to Tricophyton schoenleini) occurs in Egypt. It is seen oftener in rural areas than in cities such as Port Said. Treatment consists of softening the crusts with hot olive oil or mineral oil and epilating by means of x-rays or thallium acetate.

X-ray apparatus for epilation has only recently become available to the free clinics.

Deep Mycoses.—Mycetoma (maduromycosis) is endemic in the Sudan, whence a few cases reach Egypt. The commonest type of fungus responsible is that which produces white or yellowish-white grains (Allescheria boydii Shear). The black-grain type caused in Egypt by Cryptococcus jeanselmi and in the Sudan by Trichosporon khartoumensis is seen occasionally.[5] A red type due to an Aspergillus has been described. Our experience is limited to three cases of maduromycosis, one of which was in a Sudanese. All the patients were peasants who had the white-grain type of involvement. The lesions were limited to the feet.

Actinomycosis is very occasionally seen. The commonest causative organism is the yellow-grain-producing type, Actinomyces israeli.

Blastomycosis glutealis fistulosa (Kartulis gluteal blastomycosis) was described by Kartulis in Alexandria in 1909. The condition, as its name implies, occurs in the gluteal region as indurated subcutaneous nodules which break down to form abscesses and sinuses. Finally, a picture resembling bilharziasis of the skin is produced. Neguib Scander reported a case [7] of a closely related condition occurring in the scalp of a child; a Cryptococcus grew in pure culture from the multiple abscesses.

Sporotrichosis and blastomycosis (Gilchrist and Stokes) are on record.[6] Coccidiomycosis, histoplasmosis, rhinosporidiosis, cryptococcosis (Busse-Buschke), and paracoccidioidal granuloma have not yet been reported.

ALLERGIC SKIN DISEASES

Occurrence of eczema, contact dermatitis, urticaria, and other allergic skin diseases was somewhat over 15% in our series of clinic patients. In private practice these diseases are even more common.

Contact-type dermatitis is caused by innumerable chemical agents, such as disinfectants, antiseptics, ointments, oils, greases, acids, alkalis, dyes, paints and lacquers, cosmetics, and leather. Plant dermatitis is relatively uncommon, because many of the offending species do not grow in the country. Rhus dermatitis is rare. Mangifera indica (mango) belonging to the same family as Rhus (Anacardiaceae) is grown throughout the country. Primula, a common offender in England, is grown in some gardens. Pyrethrum is cultivated on a small scale by the Ministry of Agriculture for the preparation of insecticides. Derris root is also grown. Several plants considered to be photosensitizers are known.

7. Scander, N.: Yeast as a Cause of Disease in Egypt, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 3, Cairo, Imprimerie Nationale, 1931.

Atopic Dermatitis.—All the classic types of atopic dermatitis are seen. The commonest is the infantile variety, followed in frequency by childhood and adult types. Detection, elimination, and hyposensitization to the allergic factors pose difficult problems.

Urticaria.—The high incidence of urticaria in Egypt is probably due in part to the commonness of intestinal parasitic infestations: ascariasis, ancylostomiasis, amebiasis, and bilharziasis. Ingestants and inhalants are also causative factors. Cotton, one of the principal Egyptian crops, may produce allergic symptoms, including urticaria, by the inhalation of its dust. We have found the antihistaminics (benadryl® [diphenhydramine hydrochloride U. S. P.], antistine® [antazoline hydrochloride], neo-antergan® [pyrilamine maleate], pyribenzamine® [tripelennamine hydrochloride U. S. P.], and "anthisan" [British proprietary name for "anthallan," a proprietary coal-tar derivative]) of value for the symptomatic control of hives.

DRUG ERUPTIONS

Sulfonamides, penicillin, and crude liver extracts are among the most frequent inducers of dermatitis medicamentosa in Egypt.

Sulfonamides are still commonly dispensed and prescribed. In our experience the following types of reactions have been attributed to them: fixed drug eruptions, erythema-nodosum-like lesions, morbilliform rashes, erythema-multiforme-like eruptions, and purpura. Contact dermatitis often results from local application of sulfonamide ointments and powders.

The most frequent types of reactions to penicillin are urticaria, serum-sickness-like reactions, and erythematovesicular eruptions of the hands and feet. Contact-type dermatitis resulting from local application and handling are also seen.

Liver extracts are often responsible for urticarial eruptions. Salicylates, barbiturates, bromides, iodides, and serums are also common producers of drug eruptions.

SYPHILIS

There has been no venereal disease control legislation in Egypt until very recently. Syphilis, gonorrhea, and the other venereal diseases have not been notifiable, so we have no exact information on the incidence of these diseases. The following tabulation shows the number of new patients with syphilis reporting to the Ministry of Public Health Venereal Disease Clinics during the years 1940, 1945, 1946, and 1947.

Year	Population	Total Cases	Early Syphilis	Late Syphilis	Congenital Syphilis
1940	16,773,300	16,291	6,457	7,953	1,881
1945		12,109	5,453	5,466	1,190
1946		12,053	4,641	5,797	1,615
1947	19,040,448	10,735	4,055	5,414	1,266

Although some believe that syphilis has existed in Egypt from ancient times in sporadic form, apparently it did not assume epidemic proportions until it was spread throughout the country by Napoleon's soldiers. Previously the Crusaders were reported to have brought the disease to the country. It was commonly known as the disease of the Franks.[8] Ignorance and superstition made syphilis a scourge among the lower classes of the population until comparatively recent times. With the opening of public clinics, efforts to enlighten the people in matters of medical

care, and the introduction of arsphenamine U. S. P. and heavy metal therapy, the disease seems to have been brought under control. Available statistics from maternal and child welfare centers, where prenatal serologic tests for syphilis are supposed to be performed routinely, indicate an incidence of about 5% positive reactions in expectant mothers. The number of infants born with congenital syphilis is indeterminable, since most women are delivered in the homes by midwives.

Since the end of World War II, the number of new syphilis patients reporting to the Port Said Clinic has dropped from 386 in 1946 to 176 in 1948. The incidence of gonorrhea also seems to have declined significantly. We think that the principal reasons for the decreasing incidence of these diseases are the cessation of soldier movements and the widespread availability of penicillin. Many persons with gonorrhea are treated with large doses of penicillin (often 3,000,000 units or more) by persons other than physicians. The doses are so large that it is reasonable to believe that many cases of syphilis are aborted during the incubation period. Paradoxically, penicillin treatment of syphilis is not yet in general use. In public health clinics and physicians' offices many patients are still treated with neoarsphenamine and bismuth. The Ministry of Health, in cooperation with the World Health Organization, is planning to introduce penicillin treatment, along with other public health measures, for the control of venereal diseases.

Early infectious syphilis is usually benign. Phagedenic sores used to be very common [8] but are now seldom seen. Frambesiform secondary syphilis has also become rare. We have seen it in two cases in the past three years. In both instances the patients were desert Arabs whose entire families of five and seven members had secondary syphilis.

Most cases of syphilis are diagnosed in latency on the basis of positive reaction to Wassermann tests.

There are no reliable statistics on the incidence of symptomatic neurosyphilis. General paresis is uncommon; we have recorded only three cases in our Port Said series. Tabes dorsalis is also rare; we have had only one patient with it. We have seen only four patients with syphilitic primary optic atrophy in the last three years. Acute syphilitic meningitis and meningovascular neurosyphilis are seen in the medical wards occasionally.

There are no statistics on the incidence of cardiovascular syphilis, but it is not uncommonly encountered in medical clinics and wards.

CHANCROID

Chancroid has a comparatively low incidence. In only 15 patients was the condition so diagnosed in the Port Said Clinic during the three year period, 1946-1948, (13 males and 2 females). This low incidence may be due to the fact that ritualistic circumcision is performed on nearly all infants in the country.

LYMPHOGRANULOMA VENEREUM

To our knowledge no lymphogranuloma venereum has yet been proved to have been contracted in Egypt. During the past three and one-half years only six patients with poradenolymphitis have been seen in the Port Said Clinic. Five of the patients

8. Madden, F. C.: The Surgery of Egypt, ed. 2, Cairo, The Nile Mission Press, 1922.

were foreign seamen who had symptoms prior to landing in Egypt, and the sixth was an Egyptian who had probably contracted the disease while on a vist in Italy during the summer of 1947.

GRANULOMA INGUINALE

This disease is rarely seen (the Port Said series includes only 2 cases) although it is presumably due to an organism which is morphologically identical with that producing leishmaniasis cutis.[9]

LEPROSY

Leprosy has been an endemic disease in Egypt since ancient times. Although cases are reported from all parts of the country, the disease is most prevalent in the central parts of the Nile Delta and in Upper Egypt in the provinces of Guirga, Assiut, and Kena.[10]

Muir [11] estimates the number of patients in Egypt and the Anglo-Egyptian Sudan at about 26,000. El-Dalgamoni,[12] however, estimates the total number of victims of this disease in Egypt alone at about 30,000. More than 10,000 patients are under treatment in government-sponsored facilities. Since leprosy is rife in the southern parts of the Sudan, Muir's figure is to be considered low.

The Egyptian government has done much to control leprosy since 1929. There exist at present two leprosaria for segregation (total bed capacity, 1,500) and 46 outpatient clinics for treatment of patients and examination of their contacts. Additional clinical installations are being planned.

It is not uncommon to find leprosy patients attending dermatologic clinics. In fact, many cases are discovered in this way.

The relative frequency of the types of leprosy recorded in 10,939 cases, according to El-Dalgamoni, follows.

Lepromatous (nodular)	1,203	11%
Tuberculoid (neural)	5,251	48%
Uncharacteristic (mixed)	4,485	41%

The principal therapy until recently has been chaulmoogra oil and its ethyl esters but the sulfones are beginning to be used.

TUBERCULOSIS CUTIS

Pulmonary, osseous, and glandular tuberculosis are common in Egypt. Cutaneous tuberculosis, however, is not common. In Port Said the number of recorded new cases of pulmonary tuberculosis during the years 1946, 1947, and 1948 were 300, 361, and 359, respectively. In our series of 15,980 dermatologic patients examined during the same period, there were only 26 with scrofuloderma and 4 with lupus vulgaris. Of the tuberculides, five cases of the papulonecrotic type, three cases of lichen scrofulosorum, two cases of erythema induratum Bazin, and one case of sarcoidosis were recorded in the same series.

9. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

10. El-Dalgamoni, M. A. K.: Leprosy in Egypt, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 5, Cairo, Imprimerie Nationale, 1932.

11. Muir, E.: Manual of Leprosy, Edinburgh, E. & S. Livingstone, 1948.

12. El-Dalgamoni, M. A. K.: Personal communication to the authors, 1949.

LEISHMANIASIS CUTIS (ORIENTAL SORE)

Leishmaniasis cutis is endemic in Egypt. The causative agent is believed to be Leishmania tropica (Wright), a small (2 to 4 μ in diameter), round or ovoid organism, which is usually present in abundance in the cytoplasm of large mononuclear cells. It can be identified in smear preparations from a lesion. Ordinarily the organism is transmitted by an insect vector, the Phlebotomus papatasii mosquito, but patient-to-patient contact is known to have occurred.

The primary lesion is a brownish-red papule or nodule which may or may not undergo ulceration. The lesions, which may be solitary or multiple, occur on exposed surfaces: the face, dorsa of the hands, legs, and dorsa of the feet. They never occur on the palms, soles, or hairy scalp.

The primary lesion often eventuates in a shallow crater-like ulcer, 1 to 2 cm. in diameter (occasionally larger), with sloping ill-defined edges which show apple-jelly nodules upon diascopy. It exudes a seropurulent material which tends to crust. In some cases the nodules do not ulcerate but gradually heal by subepidermal fibrosis.

A closely related type is the chronic inflammatory form which clinically appears as a scaling or crusted flat plaque.

A lupoid type is also described. It is seen as discrete opaque brownish-red nodules which usually occur on the cheeks; they do not exhibit the apple-jelly appearance upon diascopy.

A verrucose form of cutaneous leishmaniasis is seen in Egypt. Madden [8] considered it commoner than all the other types, which he grouped together as the "flat type." These lesions usually occur on the lower extremities but may occasionally affect the forearms and hands. The initial nodules gradually proliferate into warty outgrowths which may attain a diameter of 7 to 10 cm. They are often raised as much as 1 in. (2.54 cm.) above the surrounding skin and tend to have overhanging edges. The surrounding skin may be normal or phlegmonous. In some cases there is a hypo- or hyper-pigmented areola about the lesions. By the time it is seen by a physician, the surface of the lesion is often ulcerated, in whole or in part. It is covered by hard whitish epidermis and presents a warty cauliflower-like appearance. The lesion is intersected with clefts lined with foul decomposing epidermis and purulent secretion.

Some of the initial lesions appear as boils or abscesses, usually on the face. These, too, tend to ulcerate later.

Subjective symptoms are usually minimal or absent. Occasionally there may be some pruritus in the papular stage. There may be pain if lesions occur over articular surfaces.

The lesions of leishmaniasis cutis are multiple in about half the cases. The organism (L. tropica) can be demonstrated in all the described types in tissue smears or on histopathologic section.

Histopathology.—The histopathology is so well described by Ferguson [13] that we quote it here as it appeared in Madden's Text.

Warty form:

In a section one sees a number of vertical epithelial columns, which penetrate into the dermis, sometimes to a depth of 7 to 8 mm. Structures resembling cell-nests have been frequently observed. The prickle-cell nature of the epithelial down-growths is, as a rule, very clearly seen,

13. Ferguson, cited by Madden.[8]

the intervals between the cells being rather greater than usual by reason of intercellular edema. The stratum granulosum and the keratinous layer are usually considerably increased in thickness.

The dermis is the seat of an exceedingly dense and uniform cellular infiltration, which is continuous beneath the entire extent of the lesion. This infiltration is composed of cells of various kinds. The superficial strata of the dermis, in the central parts of the lesion, frequently contain considerable numbers of polymorphonuclear leucocytes, as well as cellular detritus, the results of pyogenic infection. More deeply the infiltration is composed almost exclusively of mononuclear elements of various kinds. A certain portion of these are indistinguishable from lymphocytes. In the midst of this cellular zone, small ill-defined areas are observed, composed of mononuclear cells of much larger size than the preceding class. The parasites are found in largest numbers in the interior of the cells composing such areas, though by no means exclusively confined to them. The infiltrated areas just described are fairly vascular, considerable numbers of small vessels of capillary character being present.

Hair follicles and sweat glands have not been observed to suffer any degenerative or destructive change.

Flat form:

The skin here, in contrast to the preceding form is thinned and atrophied, the glands of the skin sharing markedly in the atrophic process. A sharply defined zone of cellular infiltration, practically identical in all respects with that described as pertaining to the warty form, is present under this thinned epidermis.

The prognosis of oriental sore is ordinarily good, but cure is at times difficult. Individual lesions usually heal without treatment within two years, the average being about nine months.

Treatment.—Antimony and potassium tartrate, administered intravenously, has given good results. More recently we have used stibamine glucoside (neostam®), an organic antimony compound, with good therapeutic results and practically no toxic side effects. Excision, refrigeration with carbon dioxide snow, and x-ray therapy are also used. We have no knowledge of the effect of the antibiotics, such as streptomycin and aureomycin, in leishmaniasis.

CUTANEOUS BILHARZIASIS (SCHISTOSOMIASIS)

Egyptians have been suffering from bilharziasis since ancient times. It is estimated that at least 52% of all Egyptians are infected.[14]

Infestation occurs by penetration of the larvae into the skin of peasants who come in contact with the cercariae-containing waters of the Nile. The cercariae are carried through the afferent circulation to the right heart, pulmonary circulation, left heart, and the systemic circulation. Those which reach the portal system produce the usual manifestations of the disease. The mature male and gravid female parasites travel coupled together in the portal system against the blood stream until the lumen of the vein allows no further progress. The female worm then leaves her partner and travels in the venules to reach the submucosa of the bladder (Schistosoma haematobium) or the large bowel (Schistosoma mansoni), where she lays her eggs. The eggs are then extruded into the hollow of the viscus and proceed on their way to the intermediate host (certain snails).

Sometimes the adult worms pass through collateral veins into the systemic veins. This results in the deposition of bilharzia ova in other tissues and organs, including the skin. The perineum, ischiorectal fossae, and the buttocks are the commonest sites for the subcutaneous deposition of Bilharzia ova. The reaction to the presence

14. Helmy, M.: Personal communication to the authors, 1949.

of the ova results in the formation of hard nodules which may undergo fibrosis or, more commonly, break down to form sinuses or fistulae. When the perineum and ischiorectal fossae are involved, fistulous tracts penetrating the urethra or rectum may form, resulting in urinary or rectal fistulae. At times a fistula may traverse a long course. Makar and Aboul Nasr [15] reported a case of a bilharzial femoral-urinary fistula extending from the posterior urethra to the upper part of the right thigh.

When the buttocks are involved, the lesions consist of extensive hard masses riddled with sinuses which exude a seropurulent discharge with a characteristic offensive odor.

Sometimes cutaneous bilharzial lesions become secondarily infected resulting in phagedena-like ulcerations. Bilharzial fistulae may be accompanied by false elephantiasis of the skin of the scrotum and penis; involvement of the labia majora also results in pseudoelephantiasis. These manifestations were more common before antimony and potassium tartrate therapy was used.

Although the incidence of bilharziasis of the skin, as well as surgical bilharziasis, has decreased significantly during the past 25 years, the disease is still prevalent. The decrease is probably due primarily to the fact that the Ministry of Health has set up bilharziasis treatment centers throughout the country. Educational campaigns directed to the people have succeeded in influencing those infected to seek treatment in the early stages.

Histopathology (Figures 1 and 2).—The cutaneous nodules are composed of bilharzial tubercles. A tubercle consists of Bilharzia ova, entire and live, or undergoing degeneration or calcification, surrounded by a localized histiocytic cellular reaction rich in eosinophils. Occasional giant cells are seen. Eosinophilic collections, termed eosinophilic abscesses, may be seen in the papillary processes, as well as in the dermis. The epidermis overlying the tubercles and abscesses is edematous. The skin appendages are affected only secondarily by the pressure of the pathologic process.

It is believed that the reaction about the ova is produced principally by a "toxin" which stimulates the formation of granulation tissue rich in eosinophils. This is based on the experimental work of Sorour [16]: Washed living ova were injected into the ear vein of rabbits, the animals were killed five or six days later, and typical bilharzial tubercles were found in the lungs. When the experiment was repeated using ova which had been killed by heating to 55 C. for 10 minutes, tubercles were not found.

In addition to the granulomatous lesions described, nonspecific cutaneous manifestations are also known in bilharziasis. They often represent the earliest symptoms of infection. As the cercariae pierce the skin, the patient experiences pruritus and other paresthesias, which are worse during the day than at night because of the increased activity of the cercariae during the hotter hours. Urticarial reactions of varying severity, sometimes with fever, are seen from four to eight weeks after infestation has occurred.

15. Makar, N., and Aboul Nasr, L.: Unusual Urinary Fistulae, J. Roy. Egyptian M. A. **30**:333, 1947.

16. Sorour, M. F.: The Pathology and Morbid Histology of Bilharzia Lesions in Various Parts of the Body, Comptes Rendus du Congrès International de Médecine Tropicale et d'Hygiène, Cairo, December, 1928, Vol. 4, Cairo, Imprimerie Nationale, 1932.

Fig. 1.—Section of skin from bilharzial granuloma of perineum. The dermis and interpapillary process show eosinophilic abscesses which contain Bilharzia ova (some live and containing miracidia; others dead and calcified); hematoxylin and eosin stain; × 72.

Fig. 2.—Granulomatous reaction in the dermis surrounding Bilharzia ova. The infiltration consists of eosinophils, plasma cells, and histiocytes; hematoxylin and eosin stain; × 114.

FILARIASIS

Wuchereria bancrofti is found in the Nile Delta, especially near the Mediterranean coast. However, clinical filariasis is limited primarily to districts which depend on wells or water reservoirs for their water source.[17]

Baz reports that a recent survey (1946) revealed a diminishing incidence of filariasis in endemic centers where newer methods of irrigation have replaced wells and water reservoirs. Illustrative of this is the town of Rashid on the Mediterranean coast near Alexandria. The disease was endemic here but has been disappearing since a community water supply replaced the water reservoirs and wells in 1936. It is not certain whether the water is a breeding place for the carrier mosquito Culex pipiens [18] or a medium for the parasite itself.

All the signs and symptoms which result from infection by the microfilaria are due to obstruction of the lymphatic vessels by the parasite or its ova. The lymphatic obstruction leads to dilatation and eventual thickening and varicosities of the vessels, with lymphedema or lymphorrhea in the obstructed area. The ultimate clinical picture depends upon the position of the lymphatic blockage, the degree and permanency of the obstruction, and the state and possibilities of the collateral channels.

Elephantiasis is by far the commonest manifestation of filariasis. It has a predilection for the scrotum, the vulva, and the lower extremities. It is the result of lymphatic blockage plus, in many instances, invasion of secondary pyogenic organisms, principally streptococci. The initial symptoms of infestation are rigors, fever (elephantoid), and lymphangitis. The last may go on to suppuration. The regional nodes are enlarged, tender, and inflamed. Following subsidence of the acute attack, the affected part remains enlarged, due to subcutaneous lymphedema. These acute episodes tend to recur at intervals of weeks to months, and the affected parts tend to enlarge with each attack. In some instances they eventually assume enormous proportions.

At first the skin over the affected area looks smooth but thickened. Sometimes it is dotted with tiny vesicles which contain and discharge lymph. In advanced cases, the skin becomes thick and rough and develops warty excrescenses. The hair follicles may become hypertrophied and stand out prominently at considerable distances from one another.

Extreme degrees of elephantiasis are uncommon in present-day Egypt. Modern therapy with antimony compounds in combination with sulfonamides and antibiotics is preventing these incapacitating complications of filariasis.

RHINOSCLEROMA

Although rhinoscleroma is another of the endemic diseases of Egypt, it is not often seen by physicians today. The bacillus Klebsiella rhinoscleromatis of von Fritsch is found in the granulomatous lesions but has not been positively incriminated as the causative agent. The disease usually starts in some part of the nose as a localized submucous or subcutaneous nodule which is of cartilage-like consistency. In the course of time, the hard granulomatous mass involves the whole nose and, frequently, the upper lip and palate as well. The growth is fairly vascular. It never softens, but it may ulcerate. Because of its size, the granulomatous mass may pro-

17. Baz, I. I.: Distribution of Filariasis in Egypt, J. Roy. Egyptian M. A. **29**:280, 1946.

18. Khalil, M.; Halawani, A., and Hilmy, I. S.: On the Transmission of Filariasis Bancrofti in Egypt, J. Roy. Egyptian M. A. **15**:317, 1932.

duce symptoms due to pressure on contiguous structures, e. g., pressure on the Eustachian tubes causing deafness and impingement on the lachrymal ducts causing epiphora. The lesions are generally painless. The disease is slowly progressive.[8]

Histopathology.—The tumor consists of dense collagenous tissue studded with plasma cells. Large phagocytic cells, first described by V. Mikulicz, and hyaline or colloid degenerated cells (Russell bodies) are characteristic elements.

The prognosis is usually unfavorable. Surgical excision, autogenous vaccines, and large doses of iodine have been used with poor results. Some cases have apparently responded to x-ray therapy.

DIPHTHERIA OF THE SKIN

During World War II, an epidemic of gangrenous-appearing deep ulcerations of the legs was seen among laborers in Port Said, Alexandria, Suez, and Cairo. The ulcers were covered with a gray-to-black membrane and had an acute inflammatory halo about them. Although initially painful, some became anesthetic later. Many of the patients were very ill, and some died of toxemia.

Bacteriologic studies revealed that the organism common to these lesions was the diphtheria bacillus. A Streptococcus and an unidentified bacillus were also found. One of us (G. R. M.) treated several patients with this condition, and on the basis of laboratory findings, clinical behavior, and response to treatment he concluded that they had cutaneous diphtheria.

The disease responded to treatment with diphtheria antitoxin and sulfonamides or penicillin. Local treatment consisted of cauterizing the ulcers with pure phenol, followed by the application of urea or magnesium sulfate emulsion in glycerin. In the several patients observed, pain was relieved, the ulcers became clean within two or three weeks, and the general toxemia was controlled by this form of treatment. Complete healing of the lesions, however, was very slow. Postdiphtheric neuritis was a frequent sequela. In some patients signs of myocarditis developed.

ANTHRAX

Although anthrax is commonly reported in Egyptian cattle, human infection is rare. During 1945 only three cases of human anthrax were recorded, while there were 165 reports of the infection in animals.[19]

PELLAGRA

Pellagra is common in Egypt, but it is only occasionally seen in dermatologic clinics. The disease occurs principally in rural areas among the hard-working field laborers. The highest incidence is in the spring and early summer.

Data collected in the investigation of certain localities in Egypt by the Permanent Committee for Nutrition of the Ministry of Public Health indicated that nutritional deficiencies and avitaminosis were due to poverty, deficient local food production, the prevalence of parasitic diseases, and ignorance. The Committee found that of 301 persons with pellagra examined in one locality, only 5 were free from parasites.[20] The same experience was reported by Ellinger, Hassan, and

19. Khalil, M.: Anthrax and the Precautions That Should Be Taken in Hides Trading in the Near East, J. Roy. Egyptian M. A. **29**:7, 1946.

20. Report of the Permanent Committee for Nutrition for the Years 1939 to 1946, Ministry of Public Health, Cairo, Government Press, 1948.

Taha.[21] They suggested that pellagra in Egypt seems to be due to the coincidence of porphyrinuria caused by parasitic intestinal infection and a deficiency of some constituent of the vitamin B_2 complex in the diet, plus some extrinsic factor, such as hard physical work in the open air, i. e., in the sun. The role of light sensitization was proved by Spies [22] when he demonstrated improvement of the general condition and the dermatologic symptoms in hospitalized pellagrins kept on a pellagra-producing diet.

Correction of dietary deficiencies and the administration of nicotinic acid brings about prompt healing of skin lesions, and improvement of gastrointestinal and mental symptoms. The usual treatment adopted in the Endemic Disease Hospitals of Egypt consists of a diet which includes three eggs and 1 oz. (28 mg.) of dried yeast daily. The patients do very well on this regimen. The fact that the patients do well in spite of intestinal parasites is due to the abundant supply of vitamin B_2 contained in these foods. To prevent recurrences, however, the infestations must be treated too.

MISCELLANEOUS

All types of precanceroses, cancers, and lymphoblastomas are seen in Egypt. These dermatoses have no features with respect to incidence or clinical manifestations which are peculiar to the locale.

Psoriasis, lichen planus, lupus erythematosus, pemphigus, and dermatitis herpetiformis are not uncommon.

Leucoderma has been known in Egypt since time immemorial; it was often confused with leprosy. For many years the Arabs have been using the seeds of a plant, Ammi majus Linn, for the treatment of vitiligo and leucoderma. This form of treatment was used by pioneer oriental doctors, such as Ibn-El-Bitar and Daoud El-Antaky. The photosensitizing properties of this plant were apparently discovered accidentally. The natives produce a powder from the seeds, ingest it, and then expose the leucodermic patches to the sun's rays. Usually an acute erythematous and vesicular dermatitis occurs in the treated sites. With subsidence of the inflammation, repigmentation is said to occur.

Professor Azer, Dermatology Department, Kasr El-Ainy Hospital, observed the results of this form of treatment in 1941. Since then the plant has been studied in the Pharmacognosy Department of Fouad I University by Prof. I. R. Fahmy and Prof. H. Abou Shady. Three active principles with photosensitizing properties, ammoidin ($C_{12}H_8O_4$), ammidin ($C_{16}H_{14}O_4$), and bergapten, were isolated. These have been investigated clinically, and favorable results have been reported by Hammouda [23] and Mofty.[24]

27 Sultan Hussein St.

130 N. Virginia St.

Dr. Samy Guirguis gave assistance on the histopathology of bilharziasis of the skin.

21. Ellinger, P.; Hassan, A., and Taha, M. M.: Therapeutic Trials on Pellagrins in Egypt, Lancet **2**:1188 (Nov. 30) 1937.

22. Spies, T. D.: Pellagra and Vitamin Deficiency, Proc. Soc. Exper. Biol. & Med. **29**:83, 1931.

23. Hammouda, Y. A.: Leucodermia in Practice, J. Roy. Egyptian M. A. **31**:437, 1948.

24. Mofty, A. M.: A Preliminary Clinical Report on the Treatment of Leucoderma with Ammi Majus Linn, J. Roy. Egyptian M. A. **31**:651, 1948.

CLINICAL STUDY OF "QUOTANE"

A New Antipruritic Drug

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PROBABLY all physicians would welcome the development of a safe antipruritic drug, for it is generally recognized that such drugs are highly sensitizing to normal or inflamed skin, often doing more harm than good. As to the effectiveness of these drugs, opinion is divided, with too few critical surveys such as those of Shelley and Melton,[1] who concluded their studies with a pessimistic view.

A new group of compounds (amino-alkoxy isoquinolines) has recently been found to possess anesthetic properties.[2] Preliminary studies on animals showed one of these drugs, SKF 538-A, or 1-(β-dimethylaminoethoxy)-3-*n*-butylisoquinoline monohydrochloride, to be relatively nontoxic and to possess (by the rabbit cornea technic) anesthetic properties 10 times those of dibucaine hydrochloride, the most effective of the other preparations compared in the studies.[3] When preliminary clinical tests revealed no tendency of the compound to irritate or sensitize intact or abraded skin, it was made available for clinical trial in ointment form.[4] This report deals with studies of the effectiveness of the ointment in relieving the itching, or burning, associated with various dermatologic lesions.[5]

Both general experience and the work of Melton and Shelley [1b] show how difficult it is to evaluate the clinical effectiveness of antipruritic drugs. The need for

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Clinical Professor (Dr. Lynch) and Clinical Instructor (Dr. Ockuly), Division of Dermatology, University of Minnesota, Dr. H. E. Michelson, Director.

1. (*a*) Shelley, W. B., and Melton, F. M.: Relative Effect of Local Anesthetics on Experimental Histamine Pruritus in Man, J. Invest. Dermat. **15**:299, 1950. (*b*) Melton, F. M., and Shelley, W. B.: The Effect of Topical Antipruritic Therapy on Experimentally Induced Pruritus in Man, ibid. **15**:325, 1950.

2. Wilson, J. W, III.; Dawson, N. D.; Brooks, W., and Ullyot, G. E.: Local Anesthetics; Aminoalkoxyisoquinoline Derivatives, J. Am. Chem. Soc. **71**:937, 1949. Fellows, E. J., and Macko, E.: Local Anesthetic Activity of a Series of Aminoalkoxy Isoquinolines, Federation Proc. **8**: (Pt. 1); 291 (March) 1949.

3. Data supplied by Smith, Kline & French Laboratories.

4. The drug was also used in lotion form and combined with menthol and camphor in ointment form, but the results of this usage are not incorporated in this report.

5. The materials used in this study ("quotane," SKF 538-A) were provided by Mr. C. W. French of the Smith, Kline & French Laboratories, Philadelphia.

adequate controls is evident; yet, when the nature of private practice makes such controls impractical, it seems reasonable that considered, critical clinical impressions should be reported. It is realized that the results reported here must be judged critically in comparison with those of better controlled investigations on the same drugs and bases, reported in other studies by observers in large clinics.

"Quotane" (SKF 538-A) was supplied for 352 clinical trials on about 250 office patients, from 195 of whom we were able to obtain a critical evaluation of the drug. In private practice, it is likely that those who experience prompt relief do not return, nor do they inform the therapist of their relief. Consequently, the results recorded are likely to be conservative, dealing only with those patients whose records are adequate. The patients were usually instructed to apply the ointment as often as necessary to obtain relief of discomfort.

The drug was available in four concentrations. With the most effective concentration, two different ointment bases were used. (The ointment bases without

Effect of "Quotane" in 195 Patients with Pruritic Disorders Associated with Various Dermatoses

Concentration of Antipruritic Agent	Number of Trials (Total, 258)	% of Total	Degree of Relief: Failure		Grades 1 and 2 *		Grades 3 and 4 †	
			Number	% of Total at This Concentration	Number	% of Total at This Concentration	Number	% of Total at This Concentration
0.15, 0.2, and 0.3% Base 1	174	67.4	39	22.4	36	20.7	99	56.9
0.5% Base 1 ‡	21	8.1	5	23.8	5	23.8	11	52.4
0.5% Base 2 §	63	24.4	13	20.6	12	19.0	38	60.3

* Slight benefit.
† Good result.
‡ Base was an oil-in-water emulsion containing an anionic emulsifying agent (sodium lauryl sulfate).
§ Base was an oil-in-water emulsion containing nonionic emulsifying agents (esters of sorbitan and polyoxyethylene sorbitan).

the isoquinoline compound were also used.) Several patients received more than one of these preparations. The table summarizes the effect of "quotane" in 258 clinical trials in 195 patients with itching or burning disorders associated with various forms of atopic dermatitis (including moist and dry, diffuse and localized eruptions), anal or vulvar pruritus (including several instances of vulvar lichen planus and lichen sclerosus et atrophicus), contact, seborrheic, and static dermatitis, dermatomycosis, psoriasis, and a few other disorders. The results were interpreted as follows.

Failure included those trials in which the eruption became worse, the itching was unrelieved, or the patient was uncertain as to whether relief had been obtained.

Relief was divided into four grades, according to degree: (1) slight or transitory antipruritic effect; (2) complete relief up to 30 minutes, or incomplete but but satisfactory relief for longer periods; (3) much improvement for several hours, or complete relief for an hour or two, and (4) complete and lasting relief for several hours.

Grades 1 and 2 were considered as "slight benefit," and grades 3 and 4 as "good" results.

The analysis of approximately half of these trials was complicated by concomitant or previous use of mild sedation, or rarely by radiotherapy and/or additional local treatment to areas of involvement other than those to which the isoquinoline compound was applied.

A more detailed analysis was made of the results obtained with the 0.5% concentration of the drug (in both bases) in our two largest groups of patients: those with anogenital pruritus (63 trials), and those with dry, localized neurodermatitis (113 trials). It was noted that good results were obtained in 81% of the patients with anal and/or vulvar pruritus and in 50% of those with localized neurodermatitis. With this relief from itching (and, presumably, lessened scratching) the eruption improved in 60% of the patients in each group. Improvement of the eruption was noted less frequently when relief was less complete. Among those patients in whom the ointment produced "good" results, most of those with anal and/or vulvar pruritus and half of those with localized neurodermatitis received no concurrent therapy. Although a record was kept of the course of the eruption in all patients who could be followed adequately, it is of little interest in an analysis chiefly concerned with the antipruritic qualities of the drug.

Analysis of the results showed that the failures of the drug seemed not to be related to the nature of the inflammation: "quotane" had apparently relieved the pruritus regardless of cause. Increased subjective or objective symptoms were not related to any particular dermatosis. The ointment was applied in 7 instances of moist dermatitis, in 13 diffuse or extensive eruptions, and in 18 instances of contact dermatitis, with effects not much different from those in dry circumscribed eruptions.

In only 4 patients did the itching become more severe, and in 10 the eruption became worse, apparently following the natural course of the disease, except for 1 of these patients who showed an acute reaction which resembled contact dermatitis.

Patch tests or subsequent clinical reapplication were tolerated well by several of these patients. The single reaction characteristic of irritation or hypersensitivity to the ointment was observed in a woman with red, swollen, and scaling neurodermatitis localized to the left occipital protuberance and the side of the neck. Subsequently, she reacted characteristically to patch tests (*a*) with the drug and its vehicle,[6] and (*b*) with the vehicle alone. She did not react to the painted application of a 1:1000 aqueous solution of the preservative (thimerosal N. F.) alone.

In a number of instances the vehicle alone was applied without other therapeutic content. Results could be reviewed in 15 trials (not included in the table) in which a therapeutic application was first made and the control application of the base followed later and results could be compared. Psychologic complications were unavoidable in this series, as the patients expected to obtain the same or better results with the nontherapeutic preparations. In one instance the vehicle was thought to give greater relief from itching. In eight cases the patient noted no difference in the results, and in six, the active drug was thought to have better results. More numerous tests and more critical analysis are necessary but cannot easily and fairly be carried out on private patients.

6. The base was an oil-in-water emulsion containing nonionic emulsifying agents (esters of sorbitan and polyoxyethylene sorbitan).

CONCLUSIONS

The results of this study indicate that "quotane" (1-[β-dimethylaminoethoxy]-3-*n*-butylisoquinoline monohydrochloride) can be applied safely to dry or moist inflamed skin. This was true with many dermatoses, even those due to contact with irritants or sensitizers. Some relief of itching was reported in 80% of 258 therapeutic applications, and "good" results were noted in 60% of the total.

In this series the greatest effectiveness was apparent in anal pruritus in both sexes and genital pruritus in females. Relief of itching was frequently accompanied with some degree of improvement in the eruption, but this was inconstant, and the healing was usually not complete.

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INTRAVENOUS USE OF PROCAINE HYDROCHLORIDE IN CONTROL OF PRURITUS

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THE PURPOSE of this paper is to report and evaluate our experience with the intravenous use of procaine hydrochloride (*p*-aminobenzol-diethylamino-ethanol hydrochloride) as a therapeutic measure to combat pruritus and facilitate healing in a group of common pruritic dermatoses. For a long time procaine hydrochloride had been used only as a local anesthetic, although August Bier,[1] in 1908, introduced a method for its intravenous use. Intravenous procaine therapy, like many other medical procedures, was introduced with a wave of enthusiasm, only to be followed by a wave of skepticism and censure which ultimately condemned its use as a dangerous procedure, temporarily discarding it as a method of therapy. After World War II, its general anesthetic properties became better known, which caused a renewed interest in its use. There soon followed published reports of its use in the treatment of pruritus of jaundice, contact dermatitis, serum sickness, exfoliative dermatitis, pruritus ani, drug eruptions, and other dermatologic manifestations.[2] At present, we have approached a period of acceptance with a sounder scientific judgment based upon more adequate laboratory studies and a wider clinical application.

Procaine hydrochloride is *p*-aminobenzol-diethylamino-ethanol hydrochloride. Structurally, procaine is closely related to diphenhydramine hydrochloride U. S. P. (benadryl®) (*β*-dimethylaminoethyl benzohydryl ether hydrochloride) and to acetylcholine. It is heat stabile (100 degrees C.) and readily soluble in water. Procaine is quickly hydrolyzed (52% within five minutes) to form *p*-aminobenzoic acid and diethylaminoethanol. The former is acetylated, and 94% is excreted in the urine within 24 hours as *p*-aminobenzoic acid, *p*-aminohippuric acid, *p*-aminobenzoyl glucuronate, and diethylaminoethanol, or even traces of procaine itself.

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2. (*a*) Lundy, J. S.: Clinical Anesthesia, Philadelphia, W. B. Saunders Company, 1942, pp. 392, 583. (*b*) Barbour, C. M., and Tovell, R. M.: Anesthesiology **9**:514, 1948. (*c*) Wilkins, R. W.: M. Clin. North America **29**:1210, 1945. (*d*) Schoemperlen, C. B.: Manitoba M. Rev. **27**:131, 1947. (*e*) Turner, J. P., and Schmidt, F. R.: Treatment of Scleroderma with Procaine, J. A. M. A. **144**:1560 (Dec. 30) 1950.

The fate of diethylaminoethanol is unknown.[3] It also has been shown that 90% of the procaine disappears from the bloodstream in 20 minutes, due to rapid hydrolysis and diffusion into body fluids.[4] Kisch and his associates[5] demonstrated that the procaine molecule is split up by an enzyme, procaine esterase. The clinical decomposition apparently takes place in the liver or plasma. Graubard and his associates[6] and State and Wangensteen[7] have described the actions of procaine as follows: (1) antihistaminic, (2) antiacetylcholine (nerve blocking), (3) direct action on the cells (especially nerve and endothelial cells), and (4) epinephrine-potentiating action. The exact mechanism of action of the antihistaminic drugs is unknown at present, but their local anesthetic effect is well known. The antiacetylcholine effect is said to be a curare-like phenomenon, both sensory and motor synapses being affected. This is the basis for the use of local or intravenous injection of procaine in causalgias, in which an antidromic reflex is the apparent cause of the pain (vasospasm-muscle-spasm cycle). The afferent and efferent stimuli are blocked by procaine, and the cycle is broken.[8] Direct effects on nerve cells may cause some of the toxic manifestations, as well as result in breaking the vicious cycle of antidromic reflexes. The potentiation of the action of epinephrine is the rationale for the use of procaine in asthma.[9] This property may be the true reason for some of the reaction thought to be due to procaine.[10]

There are definite contraindications to the use of intravenous procaine therapy which must be respected, namely, (1) definite allergy to procaine, (2) myasthenia gravis, (3) thyrotoxicosis, and (4) treatment with digitalis or digitalis-like drugs. Diethylaminoethanol, one of the hydrolyzed products of procaine, is supposed to have a digitalis-like action.[11] Two main types of reactions due to procaine may occur and deserve consideration. One, the central nervous system, convulsant type of reaction, is recognized by agitation, restlessness, tremors, momentary unconsciousness, and sleepiness beyond comfortable relaxation. These symptoms may be followed by respiratory depression or even death. The other, the allergic type of reaction, is manifested by systemic signs of dyspnea, agitation, and respiratory embarrassment. The ability of the barbiturates to abort or prevent convulsions is well known, and they are used in controlling these reactions. Animal experimentation revealed toxic symptoms following rapid injection of procaine intravenously

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6. (*a*) Graubard, D. J.: New York J. Med. **42**:2187, 1947. (*b*) Graubard, D. J.; Waldman, M. H., and Peterson, M. C.: Ibid. **48**:1693, 1948.

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10. (*a*) Richards, R. K.: Anesth. & Analg. **26**:22, 1947. (*b*) Bietrich, N. M., and Powers, N. F.: Ibid. **27**:181, 1948.

11. Krayer, O.; Farah, A., and Uhle, F. C.: J. Pharmacol. & Exper. Therap. **88**:277, 1946.

in dosage exceeding 20 mg. per kilogram of body weight or when blood level of 25 mg. per 100 cc. was exceeded.[3] Ascorbic acid deficiency decreases the toxic dose, and the administration of ascorbic acid or dextrose, or both, increases it.[10a]

The effectiveness of any form of therapy depends in part upon the amount of the drug and the rate of administration. Since at least 90% of the procaine disappears from the blood stream within 20 minutes, owing to its rapid hydrolysis and its rapid diffusion into the body fluids, Graubard and his associates [12] concluded that the amount which could be safely excreted or detoxified within 20 minutes would be a safe maximum dosage. Clinically, they found that 4 mg. per kilogram injected within 20 minutes was a minimum effective dose. This dosage they proposed as the "procaine unit" and described a "rotameter" for effectively measuring this dosage.[13] With this dosage they observed some "undesirable reactions" in a series of 2,000 injections, namely, marked dizziness, apprehension, sensations of trembling, sleepiness, and temporary unconsciousness. Kerr and Brehm [14] reported a series of 271 injections of procaine intravenously in dosage of 0.1 to 1% in 275- to-1,500-cc. solution in varied conditions. No instance of sensitivity reaction or convulsion was observed. They concluded that the objective and subjective complaints of the patients paralleled the concentration of the solution, rate of injection, and nervous stability of the patients. Trapl and Jirásek [15] reported on a series of 103 patients treated intravenously with procaine for the relief of pruritus. This group suffered from senile pruritus, pruritus of unknown origin, urticaria, acute and chronic eczematous affections, dermatitis herpetiforme, mycosis fungoides, herpes zoster, and lichen planus. They reported that the relief was, unfortunately, of short duration and that new attacks followed the cessation of treatment. In 60% of the disseminated neurodermatitis, relief from pruritus was obtained as early as the fourth injection. Daily treatments over a period of 10 to 20 days were given, consisting of 10 cc. of 0.5 to 1.0% in saline solution. The side effects were never serious and consisted of headache, dizziness, sensation of heat, drowsiness, feeling of suffocation, acceleration of pulse and respiratory rate, and temporary changes in blood pressure readings.

Our clinical experiences indicated that a dosage of 0.1 to 0.2% of procaine hydrochloride in 500 cc. isotonic saline solution was best tolerated by our patients when given over a period of 60 to 90 minutes. All patients were routinely given barbiturate medication one hour before injection. Ascorbic acid in the amount of 200 mg. was added to each infusion, as we felt it increased the resistance against toxic side effects and benefited patients with poor nutrition. When edema was present, 5% dextrose was added and removed when the edema subsided. In patients with heavy nervous irritability and fear of the infusion thiopental (pentothal®) sodium U. S. P., in dosage of 200 to 300 mg., was added to the first two or three injections. This afforded a very satisfactory approach to overcome these symptoms and allowed further treatment to be continued without incident. It produced dramatic relief of pruritus and allowed the patient to obtain the much-desired sleep. The most favorable and dramatic responses we obtained with this modified therapy

12. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. C.: Anesthesiology **8**:236, 1947.
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were in the group of generalized neurodermatitis. Each patient in our series received one daily injection. On three occasions, two daily injections were given for three successive days. The sole guide to the number of injections given any patient depended upon the relief from pruritus and the clinical improvement of the dermatosis. The minimum number of injections given was 2, and the maximum was 30. We soon learned that if relief was not forthcoming within six days, further therapy would be of questionable value. Most patients who reacted favorably to this therapy manifested relief from pruritus after the fourth daily intravenous injection. We did not encounter any evidence of addiction to the drug, and no acquired sensitivity was observed.

A survey of the available literature revealed that dangerous sequences following the intravenous administration of procaine could be avoided if proper precautions were taken. Lundy [2a] stated that in case of individual sensitivity a systemic

TABLE 1.—*Dermatoses of 181 Patients Treated Intravenously with Procaine Hydrochloride* *

Dermatoses	Total	Male	Female
Generalized neurodermatitis	48	11	37
Pruritus ani et vulvi	21	0	21
Pruritus ani et scroti	31	31	0
Acute infectious eczematoid dermatitis	21	7	14
Urticaria (penicillin)	18	9	9
Urticaria (neurogenic)	10	4	6
Angioneurotic edema	1	1	0
Dermatitis herpetiformis	1	1	0
Neurotic excoriations	2	0	2
Herpes zoster	3	1	2
Exfoliative dermatitis	4	3	1
Serum sickness	1	0	1
Contact dermatitis	4	1	3
Localized neurodermatitis	8	1	7
Seborrhoeic dermatitis	1	0	1
Pemphigus vulgaris	3	2	1
Erythema multiforme	2	1	1
Pruritus (jaundice)	2	2	0
Total	181	75	106

* Duration of dermatoses, 7 days to 21 years; age of males, 19 to 63 years; age of females, 23 to 58 years.

reaction is the only contraindication and that a preliminary skin test in such cases may bring to light a rare sensitivity. McLachlin [3d] cautioned against the possibility of individual sensitivity and advocated skin testing with an intradermal injection of 1.0 cc. of 1% procaine solution. He stated that sensitive patients manifested a local wheal reaction accompanied with systemic signs of dyspnea and agitation within a period of 10 minutes. In our series, totaling 183 patients, a preliminary skin test, as suggested by McLachlin, was performed on each patient. One hundred and fifty-one patients had previously received local procaine injections for medical or dental reasons. Twelve patients gave additional history of frequent contact exposures to procaine. Patch tests with 1% procaine solution were done on these patients, as well as intradermal testing, and reactions to patch tests were negative. Only three patients in our series manifested reactions to intradermal testing, and they will be discussed briefly. Two patients gave a marked local reaction within a period of 20 minutes and manifested symptoms of dizziness, light-headedness, tremor, and tightness in the chest. These reactions, we felt, eliminated them from treatment. The third patient reacted positively to the intradermal injection and

TABLE 2.—*Results of Intravenous Procaine Therapy in Patients with Neurogenic Dermatoses, Group 1*

Patients, No.	Diagnosis	Injections, No.	Patients: With Complete Relief, No.	With Complete Relief, Duration	Patients: With No Relief	Patients: With Temporary Relief, No.	With Temporary Relief, Duration	Remarks
48	Generalized neurodermatitis	7-21	12	3-12 mo.	12	24	2 wk.-4 mo.	25% Complete relief 25% No relief 50% Temporary relief
8	Localized neurodermatitis	7-10	2	3-6 mo.	2	4	2 wk.-4 mo.	25% Complete relief 25% No relief 50% Temporary relief
21	Pruritus ani et vulvi	7-10	4	3-6 mo.	8	9	2 wk.-4 mo.	19% Complete relief 38% No relief 43% Temporary relief
31	Pruritus ani et scroti	5-10	6	3-6 mo.	8	17	2 wk.-4 mo.	17% Complete relief 29% No relief 54% Temporary relief
10	Urticaria	7-14	2	3-6 mo.	4	4	2 wk.-4 mo.	20% Complete relief 40% No relief 40% Temporary relief
2	Neurotic excoriation	7	0	.....	2	0	.....	100% No relief
1	Dermatitis herpetiformis	7	0	.....	1	0	.....	100% No relief
121	Total.....		26		37	58		21.4% Complete relief 30.5% No relief 48.1% Temporary relief

TABLE 3.—*Results of Intravenous Procaine Therapy in Patients with Miscellaneous Dermatoses, Group 2*

Patients, No.	Diagnosis	Injections, No.	Patients: With Complete Relief, No.	With Complete Relief, Duration	Patients: With No Relief	Patients: With Temporary Relief, No.	With Temporary Relief, Duration	Remarks
14	Urticaria (penicillin)	3-7	18	12 mo.	0	0	.....	100% Complete relief
4	Out patients							
21	Acute infectious eczematoid dermatitis	5-13	8	4-12 mo.	10	3	2-6 mo.	21.1% Complete relief 46.7% No relief 14.2% Temporary relief
1	Angioneurotic edema	5	1	12 mo.	0	0	.....	100% Complete relief
3	Pemphigus vulgaris	6-12	0	.....	0	3	(Died)	100% Temporary relief
3	Herpes zoster	4-7	3	12 mo.	0	0	.....	100% Complete relief
4	Exfoliative dermatitis	12-30	1	6 mo.	2	1	3 mo.	25% Complete relief 50% No relief 25% Temporary relief
4	Contact dermatitis	5-14	1	6 mo.	1	2	3-6 mo.	25% Complete relief 25% No relief 50% Temporary relief
1	Seborrhoeic dermatitis	7	0	.....	1	0	.....	100% No relief
1	Serum sickness	4	1	12 mo.	0	0	.....	100% Complete relief
2	Erythema multiforme bullosa	14	0	.....	2	0	.....	100% No relief
2	Pruritus (jaundice)	10	0	.....	2	0	.....	100% No relief
60	Total.....		33	.....	18	9	.....	55% Complete relief 30% No relief 15% Temporary relief

manifested no systemic symptoms. Intravenous procaine therapy was given to this patient on two consecutive days. Within 20 minutes after each infusion, the patient complained of marked dizziness, apprehension, tightness in the chest, and momentary unconsciousness. The reactions were controlled with amobarbital (amytal*) sodium N. F. intravenously, and the procaine therapy was discontinued. A total of 1,780 injections were given, and reactions recorded are reported. All patients were hospitalized, and a complete medical study was made to elicit any contraindications to the drug. All infusions were carried out under the direct supervision of an anesthesiologist, which we feel added the necessary control to eliminate possible reactions which might otherwise occur in the hands of the less experienced. As our study progressed, we found this therapy could be safely carried out as an ambulatory procedure on a weekly or biweekly basis in the operation recovery room, thus eliminating hospitalization and allowing the patients to pursue their usual business or domestic duties. Topical applications were used as the occasion demanded and were continued as long as indicated.

We realize that the control of pruritus offers a dermatologic problem. This is true especially in the group of dermatoses dependent on emotional or neurogenic factors, in which change of environment, medication, or even the physician may contribute to the alleviation of subjective symptoms. These factors were taken into consideration in the evaluation of the results reported. The majority of these patients had received recognized dermatologic therapy and previous hospitalization without relief. Intravenous procaine therapy was given to 181 patients whom we classified, according to the basis of their dermatoses, as neurogenic or miscellaneous. The results achieved are evaluated in Tables 2 and 3. The addition of thiopental sodium to the infusion in generalized neurodermatitis produced our most dramatic responses. Twelve of these patients remained symptom free over periods ranging from three months to one year. The percentage of complete relief was definitely higher in Group 2, those whose dermatoses had miscellaneous bases. The failures recorded in both groups were approximately identical. Forty-five patients of the total group received subsequent intradermal skin tests with procaine at intervals of three months to one year. No evidence of acquired sensitivity was recorded in these patients.

SUMMARY AND CONCLUSIONS

One hundred and eighty-one patients were treated intravenously with procaine hydrochloride in order to evaluate its efficacy in the control of pruritus. These were divided into two groups classified, according to the basis of their dermatoses, as neurogenic or miscellaneous. Complete relief was afforded in 59 patients, 32.5%; temporary relief in 67 patients, 37.2%, and failure occurred in 55 cases, 30.3%.

From the data submitted we feel that intravenous use of procaine hydrochloride offers another approach to combat pruritus. When properly controlled, it is safe. We recommend it when other therapies fail. Our experience with reactions is recorded.

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CIRCLE STROBE LIGHTING IN MEDICAL PHOTOGRAPHY

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COLOR photography has become increasingly popular in the past decade. Many physicians, dermatologists in particular, have been quick to appreciate its importance to augment records, especially in cases with possible medicolegal significance, and as a modality for lecture and teaching purposes.

The equipment here described is unique in the field of medical photography. Variations and advantages over the conventional photographic setups created considerable interest when the equipment was exhibited at the meeting of the American Academy of Dermatology and Syphilology (December, 1950). Hence, in response to numerous requests, the following detailed description is presented.

The apparatus (Fig. 1) is designed principally for office use and consists of a sturdy base mounted on wheels which supports a telescoping standard, the camera, and an electronic flash or "strobe" light unit. This means of lighting was selected after one of us (D. J. M.), dissatisfied with the usual floodlighting method for illuminating lesions in the oral cavity, discussed the problem with an electronics technician,[1] who suggested speed lighting as a more successful means of obtaining the results desired.

The camera employed is a Rolleicord twin lens reflex model with bantam adapter and 2, 4, or 6 D. portrait lens readily attachable as desired for close-up work. The advantages of this camera selection include (1) ground-glass focusing, available when required, and (2) the use of Bantam (Eastman K828) film, which offers pictures slightly larger than the 35 mm. size. Eight exposures per roll, rather than 20 or 35, compensate to some extent for the necessary delay in factory processing which Kodachrome® film requires. The transparencies are returned in ready mounts 2 by 2 in. in size which can be used with any 35 mm. projector. The choice of camera might well have been a single lens reflex type, such as the Kine Exakta 127, or a double extension bellows model with adapter. Each has its particular advantages and disadvantages where medical photography with speed flash lighting is concerned.

The electronic flash unit ("strobe" light, speed light) operates on 110 volt A. C. (Fig. 2). It is a device which utilizes the discharge of a charged electrical condenser or capacitor through a glass tube wherein it causes the xenon gas to

1. Technical assistance in preparing this custom-built equipment and the data included in this article was rendered by Mr. Julian J. Stark, Fairfield Radio Service, 2014 Fairfield Ave., Fort Wayne 6, Ind.

incandesce momentarily to a high, and photographically very actinic, brilliance. This unit consists of (1) four condensers with a total capacity of 64 microfarads and having a power of 115 Watt-seconds when charged, (2) a transformer capable of stepping up ordinary house current to approximately 2,000 volts, (3) a flash tube (General Electric FT429) in the shape of one nearly complete circle with a diameter of approximately 3 in. (7.6 cm.). The latter surrounds the camera "taking"

Fig. 1.—Complete mobile unit operates from a standard electrical outlet.

lens and is backed by a suitable reflector. This portion of the apparatus is enclosed in a plexiglass case for protection against breakage and elimination of shock hazard.

As an additional feature, the camera, flash tube, and reflector are mounted on a base with "handle-bar" grips and adjustable guides (Fig. 3). The subject can be framed readily and the picture taken with a minimum of effort. No focusing is necessary in close-up exposures. For the less frequently required distant pictures, ground-glass focusing, measured distance, and guide-number exposure calculations of lens aperture require slightly more time and effort.

The camera and flash unit are synchronized via contact points installed in the shutter. It is essential only to insure that the latter is open during the extremely brief flash periods (approximately 1 : 10,000 second) for uniform exposure.

Circle or coaxial lighting is not new to the field of medicine. It is employed commonly with head-mirror illumination of oral and nasal cavities. The advantages are obvious. In photography of these sites and others, it provides the uniform flat

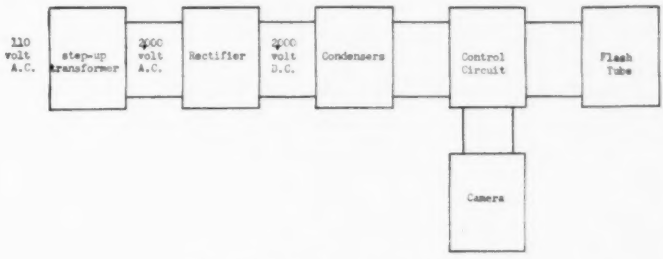

Fig. 2.—Block diagram of circuit.

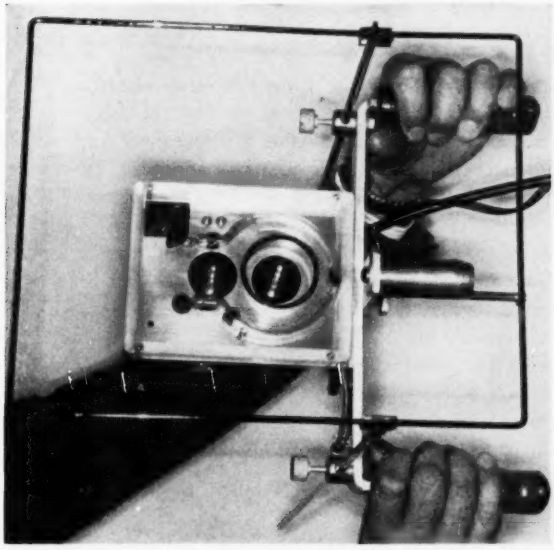

Fig. 3.—Extreme mobility of camera and light source are combined with adjustable guides to simplify the picture-taking procedure.

lighting to all visible areas so essential to color photography. There are no cast shadows. Modeling and contrast are achieved by gradual diminution of the illumination as it travels around curved objects. For example, the left side of the face receives constant uniform illumination from the left side of the tube and also a gradually decreasing amount from the right side of the tube as the light passes around the curved planes of the face. By this means, the effect of depth and roundness is created and merging of tones reduced to a minimum.

The electronic flash unit herein employed has other definite advantages. There is no heat at any time, a very objectionable feature of the customary floodlight method of illumination, especially on close-ups. Potential danger of flash-tube breakage is eliminated. The extreme speed (1 : 5,000 to 1 : 10,000 second) makes blurring from subject or camera motion an impossibility. An infant or child will neither blink nor recoil. The pupil has no opportunity to constrict. Frequently a portion of the optical fundus can be clearly visualized.

Larger condenser capacity increases the power in direct proportion. This makes it possible to take many close-ups at apertures of *f/32* or *f/22*, a factor which also increases the depth of field tremendously. In exposures of the oral cavity, the tip of the nose and the posterior pharynx are equally in clear focus.

Once the brief warm-up period of approximately 30 seconds has elapsed and an allowance of seven or eight seconds between exposures is made, the condensers are always charged to capacity regardless of minor line voltage variations; therefore, the source of light is uniform. Color temperature variations with the aging of the light source seen in the usual incandescent type of illumination are nonexistent in electronic flash lighting. The source of light, although brief, is so brilliant that other artificial light sources or daylight are overpowered; consequently, the latter can be ignored completely in proper exposure considerations. Allowance must be made for persons with light, average, or dark complexion. Variations of one-half stop are usually satisfactory.

Daylight or outdoor kodachrome® film used with electronic flash lighting will produce transparencies which suggest a slight shift of color toward the blue end of the spectrum; nevertheless, with suitable projection the variation is not apparent and color reproduction closely approaches the normal. Warmer tones, however, can be introduced if desired by the addition of the Eastman CC13 or a similar type of filter.

Beyond the initial cost, the only probable expenditure is for replacing a condenser unit. No power failure on this basis, however, has been experienced by us in over one year of service. The flash tube is good for at least 10,000 exposures as a minimum, and possibly up to 30,000 or 40,000.

SUMMARY

A new type of electronic flash lighting is described. The advantages of this method over the conventional sources of illumination in the field of colored medical photography are outlined.

347 W. Berry St. (2).

PIGMENTED NEVUS OF THE FINGERNAIL MATRIX

Report of a Case

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PIGMENTED bands of the fingernails are occasionally seen by the dermatologist, but the lesion must be rare since only three cases occurring in white persons have been reported in the literature. Two cases have also been reported in Negroes, although it would appear that this phenomenon is not uncommon among them. Ochs,[1] in 1914, described a case of a Negro woman who had multiple pigmented bands in all of the nails of each hand. In 1926, Templeton [2] reported a similar case in a Negro woman. In 1917, Montgomery [3] reported the first recorded case occurring in a white person. Two other cases, presumably in white persons, have been reported by Oppenheim and Cohen [4] in 1942 and by Oliver and Bluefarb [5] in 1944. These authors designated the lesions as a nevus striatus symmetricus unguis.

These longitudinal bands of melanotic pigment may be the origin of malignant melanomas, as shown by the case reported by Engman, Mook, and Engman Jr.[6] In their case, a fungating tumor of the tip of the left great toe occurred at the site of a wide longitudinal pigmented streak in the nail. Similar cases of malignant melanomas have been recorded in articles by Pack and Adair [7] and by Womack.[8]

In Pardo-Costello's book, Diseases of the Nails,[9] there is a section devoted to nail pigmentation, and the opinion is expressed there that the lesions are the result

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of a pigmented nevus in the matrix of the nail. Montgomery's report is in agreement with this opinion, but histologic proof is lacking in each instance. In the following case report, histologic evidence will be produced to prove this hypothesis.

REPORT OF A CASE

A 24-year-old white male physician was first observed in 1947. He had first noticed a fine brownish-black longitudinal hairline stripe at the base of the left fifth fingernail in October, 1943.

Fig. 1.—Terminal phalanx of the finger, showing the pigmented band.

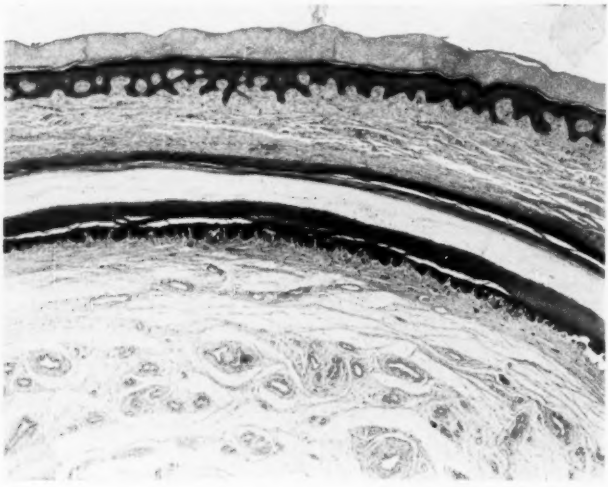

Fig. 2.—Low-power photomicrograph, showing the extent of the nevus with the normal epithelium bordering it; × 50. The nevus corresponded in size and position with the pigmented band of the nail.

This gradually progressed to the distal margin of the nail. The stripe slowly widened, and after about one year, it measured approximately 3 mm. in width. The color, however, remained unchanged during this period. In September, 1947, he first noticed that the band showed a thin darker line within the original stripe. Gradually patchy areas of deeper pigmentation developed within the band, but there was no noticeable increase in its width. The past history revealed no trauma to the fingernail. He had received no arsenical therapy except oxophenarsine hydro-

chloride U. S. P. (mapharsen®) for a fusospirochetal disease. In the summer of 1943, subsequent to the development of the fingernail lesion, he had worked in a chemical laboratory where coal-tar products were being analyzed. He had never had a pigmented mole in any other part of his body. His nails had always developed normally. There was no family history of a similar pigmented nail, and there was no family history of cancer.

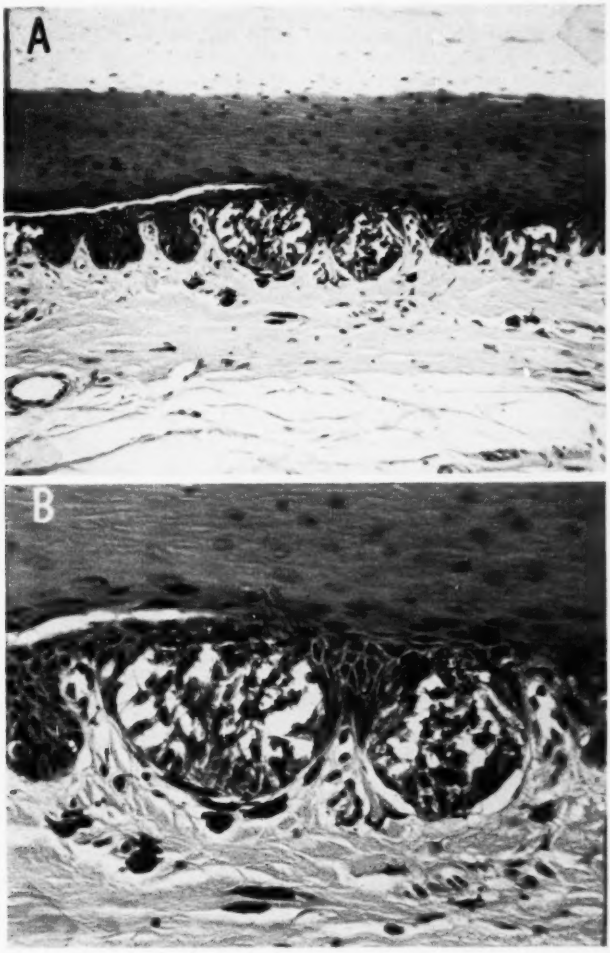

Fig. 3.—*A*, the most active areas of the nevus; × 135. *B*, detailed histologic structure of the nevus; × 350.

Findings on physical examination were essentially normal, except for the black pigmented band, 3 mm. in width, in the center of the left fifth fingernail, extending from the base of the nail to its free edge (Fig. 1). There were also two soft discrete lymph nodes in the left axilla, each measuring less than 1 cm. in diameter. The patient was seen by several consultants in dermatology, surgery, and pathology. It was the consensus that the lesion should be eliminated by amputation of the terminal phalanx of the affected finger. This procedure was done by one of us (K. A. M.) on March 24, 1948. The wound healed uneventfully.

Microscopic sections through the base of the fingernail in the region of the matrix showed a junction nevus corresponding in extent and position to the area of the pigmented band in the nail. The extent of the nevus can be seen in the low power photomicrograph (Fig. 2). With somewhat higher magnification, the character of the nevus can be seen (Fig. 3). The detailed histologic picture is well shown in a high power photomicrograph (Fig. 4). The nevus is limited to the basal epithelial cells. These cells are swollen, and they are several times the size of the normal basal cells. Their cytoplasm is vacuolated, and a few mitotic figures are seen. The papillary processes of the epidermis are enlarged and rounded, but the basement membrane is intact. Some of the epithelial cells are pigmented, and scattered cells beneath the epithelium contain brownish-black coarse pigment granules. These do not resemble the usual nevus cells but appear to be macrophages which have phagocytosed pigment.

COMMENT

This case presented an interesting diagnostic and therapeutic problem. Clinically, it was felt that the lesion represented a nevus of the nail matrix which supplied the pigment seen in the colored band of the nail. Its chronicity was thought to be indicative of a benign condition, but the gradual increase in the width of the band and the appearance of darker-pigment flecks in the band seemed to suggest increased activity of the mole. Any attempt at local excision would have destroyed the nail and left a deformed finger. It was deemed advisable, therefore, to amputate the distal phalanx of the finger in order completely to eliminate the local lesion and at the same time to allow careful histologic study to determine whether or not the lesion was cancerous. The histologic diagnosis was benign junction nevus of the matrix of the nail. This case was later reviewed by Dr. George Pack of Memorial Center for Cancer and Allied Diseases in New York. He concurred in the diagnosis and therapy.

SUMMARY

A case of benign junction nevus of the fingernail matrix is presented. The patient is well, with no evidence of local recurrence or metastases three years after amputation of the finger. The axillary lymph nodes described in the physical examination are, at the present time, the same size as when they were first observed in 1947.

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KELOID RESULTING FROM A POSITIVE PATCH TEST

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BECAUSE a question exists as to whether a keloid can arise as a result of a positive reaction to patch test, the following observation seems worthy of reporting.

REPORT OF A CASE

M. S., a white, fair-skinned, blue-eyed, 22-year-old woman, who was employed as a research chemist in antibiotics by a pharmaceutical manufacturer, was referred to me for an initial examination on May 24, 1949. History revealed that she had entered the service of this company on May 7, 1948, and had been assigned to her present specific duties on Jan. 20, 1949. In this latest occupation, for the first time and on intermittent occasions, she handled a new English antibiotic which was designated patulin (an antibiotic substance obtained from Penicillium patulum) and which was under research investigation in her department at that time. On about May 17, 1949, and after contact with the above substance, itching and burning with redness developed on the cheeks, several finger webs, both elbow bends, left wrist, and both orbital areas. In the last-mentioned location, it was early associated with swelling. During the following week end and while away from work, the process improved. Other general history was unrevealing.

Upon examination, she showed a faintly pink, finely papular, mildly scaling eruption involving the cheeks, the outer canthus of both eyes, the dorsum of several finger webs, both cubiti, and the dorsum of the left wrist beneath her watch band. No abnormal findings were noted elsewhere.

On May 24, 1949, patch tests with her occupational contactants were placed on the upper back. These were penicillin, streptomycin, and patulin. The patches were lifted 48 hours later, and at the location where the patulin lay there was a dime-sized area of redness, intense edema, vesiculation, and erosion. This was limited solely to the area contacted by the substance, and there was no tendency to local spread or new eruption in other areas. Reaction to the other two patch tests was negative.

Treatment consisted of avoidance of soap in the affected areas and application of a phenolated bland shake lotion. She was left in the same work but with advice to avoid the offender. On June 4, 1949, she was completely clear.

On May 9, 1950, she returned complaining of a single itching raised lesion on the left shoulder. She believed this to be located at the site of the earlier positive reaction to patch test with patulin. According to her statement, this earlier reaction healed uneventfully, but after a few months she had a new onset of itching in this area. Shortly thereafter she noted that the surface seemed elevated at this point. Instead of subsiding, these symptoms progressed, and she then sought advice.

Her record revealed that this lesion was at the point of her former violent patch reaction. On examination, she presented a dime-sized, irregularly shaped, solid skin tumor of the upper outer section of the right back area. This lesion further showed a distinctly elevated, uniformly reddened, smooth-surfaced, definitely firm center, with a surrounding zone of radiating, contract-

From the Department of Dermato-Syphilology of Indianapolis General Hospital, The Alembert Winthrop Brayton Skin and Cancer Foundation, and its allied P. C. Reilly Laboratory of Mycology, John Eric Dalton, M.D., Chairman.

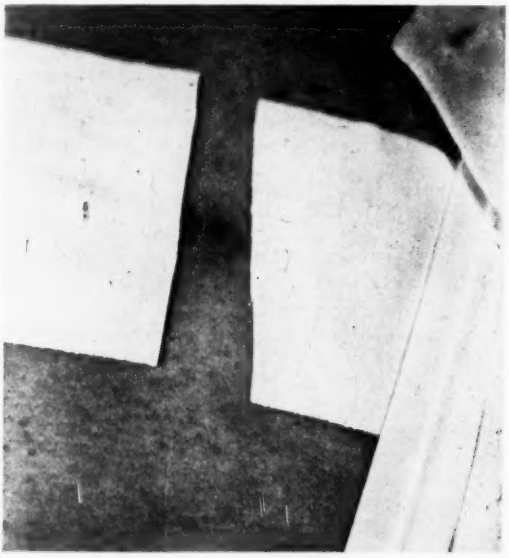
ing, whitish scar. Inspection of an earlier vaccination site, of the healed line of a previous appendectomy wound, and of other areas of previous cuts or scratches failed to show evidences of a keloidal tendency.

The lesion was excised, the edges carefully brought together, and this line treated by fractional doses of x-rays during its healing period. On Dec. 8, 1950, she was discharged as recovered.

Sections of the excised material showed the presence of a rather well delimited area of hyperplasia of cells resembling fibrocytes. In some areas the cells were round and had an elongated basophilic cytoplasm. In other areas the nuclei were smaller, elongated, and associated with a scanty cytoplasm but abundant intercellular fibrillar collagenous material. There was no active inflammatory reaction, although at the periphery of this lesion a scant perivascular infiltration of lymphocytes was noted.

The diagnosis was fibrosis of the dermis resembling keloid.

Patch tests with patulin were done on three other persons as controls, but none of them showed any reaction.



Keloid between bands of adhesive tape which were placed to give contrast.

COMMENT

Certain persons have a peculiar tendency to form a tumor-like fibrous outgrowth at the site of a previous skin trauma. Outgrowths of this kind are usually designated as keloid, although Trusler and Bauer [1] make a distinction between hypertrophic scar and keloid on the basis of regression or persistance of the lesion. Accidental cuts, scratches, or puncture wounds, surgical incisions, and vaccination needling are regarded as the injuries which most commonly initiate such a picture. However, in spontaneous keloid, we see this condition occur as a result of continued irritation to or persistent infection in a certain location. It is repeatedly pointed out that this is more likely to occur in persons with dark skin, but we all also know

1. Trusler, H., and Bauer, T.: Keloids and Hypertrophic Scars, Arch. Surg. **57**:539-552 (Oct.) 1948.

that it happens, with less frequency, in persons with light coloring, as reported here. Furthermore, it is the experience of most clinicians who have watched patients with keloidal tendency that this tissue reaction to injuries will not develop consistently. On the basis of this observation, I explain the finding that previous vaccination, surgery, and scratches had not led to excessive scar formation in this patient.

The authors mentioned above [1] believe that a keloid results only when there is both epidermal and dermal damage. Marshall and Rosenthal [2] advanced the theory that there must be an intense tissue edema with increased circulating fibrin in the background of this type of lesion. In an intense patch reaction such as occurred in this patient, it is certainly conceivable that there were both epidermal and dermal injury and intense tissue swelling.

SUMMARY

A case is presented in which a keloid resulted from a severe reaction to patch test with patulin.

23 E. Ohio St.

2. Marshall, W., and Rosenthal, S.: Pathogenesis and Experimental Therapy of Keloids and Similar Neoplasms in Relation to Tissue Fluid Disturbances, Am. J. Surg. **62**:348-357 (Dec.) 1943.

TREATMENT OF EXFOLIATIVE DERMATITIS WITH CORTISONE

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ALTHOUGH numerous reports [1] concerning the use of cortisone in the treatment of various types of dermatitis have been published, a review of the literature indicates that treatment of exfoliative dermatitis with cortisone has not been specifically elaborated. The following data on three patients treated with cortisone is being presented both because of the paucity of actual case reports and because of the successful results obtained in these patients, all of whom had been treated unsuccessfully with the usually prescribed medications. The drug was administered intramuscularly in all cases.

REPORT OF CASES

CASE 1.—J. F., a 55-year-old white man, presented exfoliative dermatitis secondary to chronic eczematoid dermatitis and dermatitis venenata. He was admitted to the medical ward Dec. 27, 1950, because of an acute, severe exfoliative dermatitis of the entire body. He had been released previously from the hospital in a state of remission from a manic phase of a manic-depressive psychosis. On the present admission, he gave the following history. For years, he had had marked perspiration of the hands and repeated episodes of eczema of the extremities. In July, 1950, after painting and using turpentine, an erythematous, maculopapular, pruritic dermatitis of the hands developed. He was treated with calamine lotion and ultraviolet rays, but the lesions failed to heal. The lesions spread to the legs, after which his physician treated the dermatitis with aluminum acetate solution soaks, an ointment of unknown composition, and vitamin B complex.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of her own study and do not necessarily reflect the opinion of the Veterans Administration.

1. Engelman, E.: Cortisone in Collagen Diseases and Other Disorders, Bull. Univ. California M. Center **11**:12-17 (Oct.) 1950. Irons, E. N.; Ayer, J. P.; Brown, R. G., and Armstrong, S. H., Jr.: ACTH and Cortisone in Diffuse Collagen Disease and Chronic Dermatoses; Differential Therapeutic Effects, J. A. M. A. **145**:861-869 (March 24) 1951. Cannon, A. B.; Hopkins, J. G.; Andrews, G. C.; Colfer, H. F.; Gross, P.; Nelson, C. T., and Howell, C. M., Jr.: Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of the Skin, ibid. **145**:201-206 (Jan. 27) 1951. Soffer, L. J.; Levitt, M. F., and Baehr, G.: Use of Cortisone and Adrenocorticotropic Hormone in Acute Disseminated Lupus Erythematosus, Arch. Int. Med. **86**:558-573 (Oct.) 1950. Behrman, H. T., and Goodman, J. J.: Skin Complications of Cortisone and ACTH Therapy, J. A. M. A. **144**:218-221 (Sept. 16) 1950. Carlisle, J. M.; Gibson, A., and Schmatolla, E.: Cortisone, Postgrad. Med. **8**:113-124 (Aug.) 1950. Brunsting, L. A.; Slocumb, C. H., and Didcoct, J. W.: Effects of Cortisone on Acute Disseminated Lupus Erythematosus, Proc. Staff Meet., Mayo Clin. **25**:479-482 (Aug. 16) 1950. Thorn, G. W.; Forsham, P. H.; Frawley, T. F.; Hill, S. R., Jr.; Roche, M.; Staehelin, D., and Wilson, D. L.: The Clinical Use of ACTH and Cortisone, New England J. Med. **242**:783-793 (May 18); 824-834 (May 25); 865-872 (June 1) 1950. Tomlinson, C. C., and Cameron, O. J.: An Analysis of Basal Metabolic Rate and Blood Cholesterol Determinations, Arch. Dermat. & Syph. **59**:22-30 (Jan.) 1949. Welton, D. G.: Exfoliative Dermatitis and Hepatitis Due to Phenobarbital, J. A. M. A. **143**:232-234 (May 20) 1950.

The condition progressed, spreading in patches over the entire body. Lesions were vesiculopustular, fissured, and crusting. The patient was afebrile. When he presented himself to the hospital, the condition was in the acute stage of exfoliative dermatitis. Desquamation was most marked on the extremities. The epidermis of the hands was exfoliating in an almost glove-like fashion. Although the patient was not toxic, he complained bitterly of intense itching.

Because of the acuteness of the disease and unsuccessful previous treatment, cortisone therapy was initiated, in a dosage of 100 mg. twice a day, Dec. 29, 1950. Within 24 hours the intense itching had subsided, the face was clearing, and the erythema of the trunk and extremities had faded considerably. On Dec. 30, he received 100 mg., followed by 50 mg. on Dec. 31 and 25 mg. on Jan. 1, 1951. Because of an intensification of pruritus and erythema, the dosage was increased to 100 mg. on Jan. 2. This dosage continued through Jan. 4, at which time medication with cortisone was discontinued. All lesions disappeared, desquamation was complete, and the patient had a soft, pink, baby-like skin. Because of dryness of the skin, his body was anointed each day with ointment consisting of boric acid solution, anhydrous wool fat, and zinc oxide paste. On Jan. 23, the skin lesions had completely healed, and there have been no recurrences to date.

CASE 2.—W. D., a 53-year-old white man, had exfoliative dermatitis secondary to stasis dermatitis and dermatitis medicamentosa. This patient was admitted to the hospital in September, 1937, with a diagnosis of psychosis, intoxication, and alcoholic deterioration. His physical condition was satisfactory until April, 1945, when a routine chest roentgenogram revealed that he had active pulmonary tuberculosis, the diagnosis being confirmed by the finding that sputum was positive for the bacillus of tuberculosis. The patient was treated with bed rest and reached an apparently cured stage, which has been maintained to the present time.

On Dec. 29, 1950, the patient was found to have a small superficial ulcer on the lateral aspect of the right ankle. Sulfathiazole ointment was applied locally, and the patient was given 300,000 units of penicillin intramuscularly for two doses. By Jan. 1, 1951, the ulcer appeared deeper and larger, and there were erythematous, macular lesions of both legs. Sulfathiazole ointment was discontinued on this date, and tripelennamine (pyribenzamine®) hydrochloride ointment was applied. By Jan. 9, the patient had developed a generalized maculopapular dermatitis which became vesicular, pustular, weeping, and finally exfoliative. Edema of the face was present.

The patient was admitted to the medical ward on Jan. 12 with an acute, severe, exfoliative dermatitis complicated by an acute, severe pyogenic dermatitis. He appeared toxic and acutely ill, although rectal temperature was only 100 F. All previous medications were discontinued. Aureomycin hydrochloride, 250 mg. orally four times a day, was prescribed; continuous aluminum acetate solution soaks were used on the hands and face. A severe epidermophytosis with maceration between the toes was present, and potassium permanganate soaks were used for the feet. By Jan. 17, the secondarily infected lesions had cleared, but the generalized exfoliative dermatitis was unimproved and severe. Cortisone therapy was initiated and carried out as follows: Jan. 19, 100 mg. three times a day; Jan. 20, 100 mg. twice a day; Jan. 21, 100 mg.; Jan. 22, 50 mg., and then 25 mg. daily for three days. As with Case 1, marked improvement was seen within 24 hours. The edema of the face subsided along with the erythema. Improvement continued, and on Feb. 5 he was returned to the psychiatric ward. He has been symptom free to date.

CASE 3.—J. F., a 62-year-old white man, had exfoliative dermatitis secondary to recurrent stasis dermatitis and dermatitis medicamentosa. He was admitted to the hospital Dec. 15, 1930, with diagnoses of (1) dementia paralytica and (2) tuberculosis, pulmonary, chronic, minimal, healed. His physical condition was satisfactory until March, 1949, when he had an acute severe stasis dermatitis of both legs. He was treated with sitz baths and petrolatum pressure dressings with some improvement, but the condition remained chronic. From that time until admission to the medical ward, the patient had had six exacerbations and had been treated by saphenous ligation, elastoplast® boots, phenindamine (thephorin®) and tripelennamine hydrochloride ointment locally, aluminum acetate solution soaks, and diphenhydramine (benadryl®) hydrochloride orally. All treatment was unsuccessful in eliminating the dermatitis. This patient was a problem of management in that he persisted in excoriating his extremities and trunk to the point of marked bleeding. On admission to the medical service, Dec. 15, 1950,

the dermatitis was confined to the face, extremities, and chest. The lesions were maculopapular, erythematous, vesicular, and weeping. Diphenhydramine hydrochloride was administered intravenously, and phenindamine ointment was applied locally. Within a week, the dermatitis had spread over the entire body, and exfoliation was taking place. On Dec. 26, cortisone medication was initiated and administered as follows: 200 mg. twice on the first, second, third, and fourth days; 100 mg. on the fifth day, and 50 mg. on the sixth and seventh days. The dosage was reduced to 25 mg. on the eighth, ninth, and tenth days. Treatment was terminated Jan. 4, 1951. The patient's condition improved until Jan. 2, 1951, when urinary retention developed owing to cord bladder, making it necessary to insert an inlying Foley catheter. Penicillin was given prophylactically to avoid cystitis. Despite this, his temperature became elevated, and urinalysis indicated a urinary infection, the urine culture exhibiting a gram-negative nonsporing rod. The patient was given gantrisin® (a sulfonamide compound) in place of penicillin. Four days later, he suffered an acute exacerbation of the dermatitis with a maculopapular, erythematous, pruritic eruption over the entire body. In view of the possibility that the patient had a dermatitis medicamentosa caused by gantrisin,® use of the drug was discontinued, and the patient was given 12.5 mg. of cortisone daily for five days. This produced no improvement. On the sixth day of medication, dyspnea and edema of the face developed, and the dermatitis became exfoliative. Within 24 hours complete exfoliation of the mouth had occurred. The dosage of cortisone was then increased to 100 mg. daily. This dosage was repeated for five days, then reduced to 25 mg. for the following seven days. As with the first course of cortisone, response to the larger doses was dramatic. The edema of the face, the dyspnea, and the erythema disappeared within 18 hours, desquamation continued, and the patient's recovery from that time was uneventful. Approximately two weeks later a transurethral resection was done with no untoward signs or symptoms. There has been no recurrence of the dermatitis to date, and the skin remains entirely clear.

COMMENT

In these three patients with exfoliative dermatitis, the period of administration of cortisone varied from one to five weeks. No toxic effects were noted; recovery from the dermatitis was dramatic. Of secondary interest, two of the patients were actively psychotic, and one was in remission from a manic-depressive psychosis. The actively psychotic patients showed slight mental improvement in that they appeared more cooperative and less clouded. The patient in remission from a manic-depressive psychosis showed no reactivation of the psychosis. Attention is also brought to the need for adequate dosage of cortisone for effective results.

LEPRA REACTION: ITS TREATMENT WITH DIHYDROSTREPTOMYCIN

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HABANA, CUBA

ACCORDING to Lara and Rodríguez,[1] lepra reaction is manifested by the appearance of multiple acute or subacute, local or systemic phenomena during the chronic course of leprosy. In some cases, lepra reaction may be the first clinical manifestation of the disease. These acute inflammatory changes, which affect different organs and almost invariably the skin, are usually accompanied with fever, on the basis of which Vandyke Carter,[2] Montañes,[3] J. M. Fernández,[4] and others have designated this reaction as "lepra fever."

Typical relapsing lepra reaction is characterized by acute constitutional symptoms, the severity of which is usually a major feature, although the symptoms may vary more or less in degree in different cases. These symptoms are in no way different from those observed in various infectious diseases, continuing throughout the duration of the process and consisting of a prodromal stage, a period of invasion, then acme, and finally a decline in severity in the stage of regression. The fever is accompanied with chills, malaise and prostration, headache, vomiting, tachycardia, tachypnea, and pains in the bones and joints, preceded or accompanied with a more or less generalized eruption. In severe cases, extracutaneous inflammatory manifestations may be observed, consisting of lymphadenitis, hepatosplenomegaly, orchitis, neuritis, iridocyclitis, keratitis, and ulceration of the nasal septum.

The eruption of lepra reaction appears as nodules, erythema multiforme and erythema nodosum lesions superimposed upon previous macules, infiltrations, and erythema, as well as in normal skin. Muir [5] remarks that all lepromatous areas are simultaneously edematous, turgescent, and inflamed; in other cases, they may be initially limited to one or two areas, gradually involving the remaining preexisting lesions.

The infiltrations vary in size, shape, and degree and are painful to pressure; their color changes from various shades of red to violaceous, sepia, or yellow-brown. One main characteristic is that all the various types of lesions are sharply limited,

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Read at the Seventy-First Annual Meeting of the American Dermatological Association, Hot Springs, Va., May 25, 1951.

1. Lara and Rodríguez, cited by Araujo, A. de S.: Lepra em quarenta paises, Trabalho do Instituto Oswaldo Cruz, Rio de Janeiro, 1929, pp. 155-179.

2. Carter, V., cited by Lewers, A.: A Note on Leprous Fever, Brit. J. Dermat. **11**:399, 1899.

3. Montañes, P., and Negro, E.: Tratamiento de la lepra reacción con piramidón, Publication of the National Sanitorium of Fontilles, Spain, 1932, p. 133.

4. Fernández, J. M.: El cuadro clínico de la reacción leprosa, Semana méd., p. 19, 1933.

5. Muir, E.: Manual of Leprosy, Baltimore, Williams & Wilkins Company, 1948.

yet even areas of apparently normal skin present a slight but distinctive erythema. After a variable length of time, the infiltrations diminish, the lesions flattening down to the original skin level, their color fades, and finally some may completely regress. In rare instances, however, the reaction may be so severe that all the skin becomes involved, assuming the appearance of a generalized erythroderma. One feature is prominent, namely, that after the reaction has subsided, the patient presents a decidedly more lepromatous appearance than previously.

The character and evolution of the symptoms in lepra reaction suggest a classification into two forms: (1) the classic type, accompanied with severe relapsing febrile episodes, and (2) atypical lepra reaction, in which febrile attacks are usually lacking. However, if febrile attacks do occur in the second form, the fever is of slight degree, although local manifestations are always present. The beneficial influence observed in the course of the disease in patients in whom the leprotic reaction is accompanied with relapsing lesions of erythema multiforme and nodosum must be emphasized. In these cases, ocular lesions but rarely occur. Conversely, the lesions of erythema nodosum or multiforme are not observed in patients with severe, long-standing, and successively recurring lepra reaction.

As previously noted, fever is the outstanding symptom of lepra reaction and is characteristic of severe types of reaction when sustained and high, that is, at levels of 102.2 F. to 104 F. or above. In atypical forms, the temperature elevation is less, from 99.5 F. to 100.4 F., and, in some instances, it may be totally lacking. As a rule, the pyrexia is remitting in character, or it may be continuous or intermittent, the fever persisting from 10 to 30 days, lasting on occasion for weeks and even months despite all therapeutic measures. Relapses are sometimes frequent with short remissions. Prolonged reactions, occurring as relapses after short intermissions, aggravate the course of the disease.

Fatal termination has been reported by Bechelli and Costa Valiente[6] and by Fidanza and Schujman.[7] I observed one myself, over 30 years ago. L. Souza Lima,[8] however, states that he has not seen a fatality in this condition.

Positive reactions to lepromin tests (Mitsuda-Rost), indicative of a high degree of specific immunity and defense reaction, are never elicited, since these patients lack immunologic resistance. This is constantly observed in tuberculoid leprosy and in some cases of the nonspecific type representing transitional forms of the infection. Large numbers of bacilli are seen in the smears. The erythrosedimentation index is also greatly increased, the rate reaching 80 to 120 mm. per hour, indicating a serious prognosis.

Lepra reaction is observed not only in lepromatous leprosy, but also in the tuberculoid variety. Wade[9] was the first to call attention to this phenomenon in 1934, and it has been reported also by J. M. Fernández,[10] Schujman,[11] and Souza

6. Bechelli, L. M., and Costa Valiente, E.: Influencia da reâçao leprótica na marcha das lesoes cutaneas da lepra, Rev. brásil. leprol. **5**:167, 1937.

7. Fidanza, E. P., and Schujman, L.: Lepra Reaction, Actual. méd. **23**:19, 1933.

8. Souza Lima, L., and Maurano, F.: Reação leprótica, Rio de Janeiro, 1949, p. 141.

9. Wade, H. W.: Tuberculoid Changes in Leprosy: Lepra Reaction in Tuberculoid Leprosy, Internat. J. Leprosy **2**:279, 1934.

10. Fernández, J. M.: La reacción leprosa tuberculoide, Rev. méd. **2**:105, 1937.

11. Schujman, L.: Tuberculoid Lepra Reaction, Internat. J. Leprosy **5**:77, 1937.

Campos,[12] who established the differentiation between tuberculoid lepra reaction and reactional tuberculoid leprosy, a variety of which was called "acute tuberculoid leprosy" by Ryrie.[13]

Lepra reaction is also observed in classic marginated tuberculoid leprids which present a flare-up of preexisting lesions which may or may not be accompanied by new tuberculoid elements, namely, nodules, papules, and plaques. In certain apparently normal persons, lepra reaction may constitute the initial manifestation of the disease. According to J. M. Fernández [10] and other authors, general disturbances are not observed in any of the stages of lepra reaction in patients with the tuberculoid variety. Following regression of the skin lesions, a more-or-less-pronounced desquamation takes place, resulting in the disappearance of congestion and infiltration, and the skin then has the same appearance as it had before the onset of the reaction.

The duration of the tuberculoid leprotic reaction is quite variable. Lowe [14] has recorded instances in which the clinical history revealed episodes of activity and quiescence over a period of 50 years. The smears in patients with tuberculoid leprotic reaction almost always fail to show the Mycobacterium leprae, and the erythrosedimentation rate remains unaltered, these features serving to aid in the differentiation from tuberculoid reactional leprosy. The prognosis is good, except for those patients in whom the large nerve trunks are involved, with associated muscular impairment.

The status and interrelations of the reactional processes observed in the evolution of leprosy have been firmly established since the adoption of the Pan-American classification by the Fifth International Leprosy Congress in Habana, April, 1948. Nevertheless, the exact nature of the process has not been determined, although the differences and delimitation in the clinical evolution of the lepra reaction in the lepromatous, tuberculoid, and undifferentiated types are evident.

In the treatment of this reaction, control of only the lepromatous patients is important because of the serious prognosis and the resistance to all therapeutic methods in some cases, in contrast to the benign course and spontaneous cure in patients with the tuberculoid type. The latter patients have no subjective symptoms, and the therapeutic results are excellent. On the contrary, patients presenting the lepromatous lepra reaction suffer not only from severe constitutional disturbances but also from persistent fever and serious, intractable ocular and neurologic lesions. For these reasons, leprologists have used various methods and a large number of drugs in the treatment of such patients.

In spite of recent advances in the field of leprology, the pathogenesis of lepra reaction remains as yet unknown, and its role in the evolution of the disease is still the subject of much debate. Some authors admit the necessity for its treatment, while others oppose this view, accepting the reaction as beneficial to the further course of the disease.

On the other hand, it cannot be denied that, in the majority of cases, the distressing condition of the patient, including the prolonged hyperpyrexia and the

12. Souza Campos, N.: Lepra tuberculoide reaccional, Rev. brasil. leprol. **8**:45, 1940.

13. Ryrie, G. A.: Acute Ulcerative or Sloughing Tuberculoid Leprosy, Internat. J. Leprosy **6**(2):153, 1938.

14. Lowe, L.: Study of Leprosy Macules, Particularly of Tuberculoid Macules, Lepra in India **2**:18, 1937.

various associated serious complications, call for efforts to develop effective therapeutic measures for their relief. These, however, in view of our present lack of exact data concerning the pathogenesis of the process, must of necessity be based upon only hypothetical grounds, and thus are merely empiric and symptomatic in nature.

In general, it may be stated that the use of various drugs and other proposed therapeutic methods are based upon the following theoretic considerations: (1) counteraction of the possible untoward effects of previously administered drugs, namely, chaulmoogra and the sulfones, as factors in the production of the lepra reaction; (2) alleviation of the allergic status of the patient; (3) improvement of the general condition of the patient; (4) control of possible coexisting infections, specific or nonspecific, and (5) reactivation of the reticuloendothelial system.

So many drugs and different methods have been recommended for the treatment of lepra reaction that it would be manifestly impossible to enumerate and evaluate all of them. Some are known to be capable of achieving temporary clinical improvement but do not prevent subsequent relapses. In other cases, these methods have proved to be ineffectual primarily during the initial development of the reaction, as well as later during episodes of relapse.

Although encouraging results have been observed in the treatment of leprosy with the sulfone drugs, the use of which has reduced the incidence of lepra reaction, a not inconsiderable number of cases are still encountered. In many of these cases the condition cannot be controlled by the administration of either antimony potassium tartrate, stibophen, or other recommended chemical agents, or by partial or complete discontinuation of the sulfone drugs.

To overcome the deficiencies of the sulfones, G. H. Faget and P. T. Erickson [15] attempted for the first time to treat leprosy with streptomycin in April, 1947. The rationale of this new therapy was the remarkable healing observed in a patient with laryngeal tuberculosis treated with streptomycin, reported in 1945 by Hinshaw and Feldman.[16] Faget and Erickson treated 10 selected lepromatous patients with a four months' course, giving 2 gm. of streptomycin every 24 hours. After four months, they decided to prolong the therapy for another similar period, the dosage, however, now being reduced to 1 gm. per day. According to these authors, the results were encouraging. They noted, however, that the drug was too toxic and its mode of administration too disturbing to the patient, and they expressed the opinion that unless it could be further purified to decrease its toxicity or its effective therapeutic dose reduced streptomycin would probably not become the treatment of choice for leprosy.

Dreisbach,[17] at the Palo Seco Leper Colony, C. Z., Panama, contributed the first report on the use of streptomycin in five lepromatous patients manifesting lepra reaction, whose clinical course was not influenced by the sulfones or other methods usually employed. Although favorable results were noted in two of these patients, the author did not draw any definite conclusions. Arturo Romero and

15. Faget, G. H., and Erickson, P. T.: Use of Streptomycin in the Treatment of Leprosy, Internat. J. Leprosy **15**:146, 1947.

16. Hinshaw, H. C., and Feldman, W. H.: Streptomycin in Treatment of Clinical Tuberculosis: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **20**:313, 1945.

17. Dreisbach, J. A.: The Use of Streptomycin in the Treatment of Lepra Reaction, Report of the 5th International Congress on Leprosy, Habana, 1948, p. 259.

Abelardo Brenes Ibarra,[18] in a short communication to the Fifth International Leprosy Congress, reported the good results obtained with small doses of streptomycin (3 to 5 gm.) in five lepromatous patients with lepra reaction.

O. Romero and J. Grau Triana[19] substituted the newer antibiotic, dihydrostreptomycin, for the streptomycin which had proved to be toxic in its effects, administering it to four patients with lepra reaction of the lepromatous type after they had failed to respond to the ordinary routine methods of therapy. The dose employed was 1 gm. per day, divided into four injections given one every six hours over periods of from 8 to 20 days. The results were reported as excellent: The fever subsided, the general symptoms disappeared, the cutaneous lesions rapidly regressed, and the erythrosedimentation rate decreased.

Since streptomycin[20] has been found to be useful for patients who appeared to have reached a limit of improvement in skin and mucous-membrane lesions with sulfone therapy, and since it seems to have the ability to effect a reduction of the Mycobacterium leprae in the lesions, the use of this antibiotic would appear to be indicated in the treatment of lepra reaction. Dihydrostreptomycin, however, has replaced streptomycin because of better tolerance and lower toxicity. Dihydrostreptomycin is a valuable drug in the treatment of lepra reaction, provided that dosage and duration of administration are properly determined in order to preclude possible untoward reactions.

Dihydrostreptomycin was administered to three lepromatous patients manifesting severe relapsing lepra reaction in whom the various drugs and other therapeutic methods usually recommended for this condition had failed to produce improvement. Subsequently, six additional patients were treated with dihydrostreptomycin alone. The results in these nine cases, demonstrating the beneficial effect of this antibiotic in the treatment of lepra reaction, constitute part of the basis of this report.

The patients receiving dihydrostreptomycin were given the daily amount of 2 gm. intramuscularly in three divided doses every eight hours over periods of from 10 to 20 days. The clinical course was followed by means of routine laboratory studies, which included blood examination, smears taken from nasal mucus and lepra lesions, the erythrosedimentation index, and the lepromin test. During and following dihydrostreptomycin therapy, smears of skin lesions and nasal mucus showed a decrease in the number of acid-fast bacilli. A reduction in the erythrosedimentation rate was also observed.

Neither vertigo, fever, skin eruptions, and renal irritation nor the more serious complications of tinnitus, impaired hearing, and exfoliative dermatitis were encountered in any of the patients treated with dihydrostreptomycin.

Since dihydrostreptomycin was found to enhance the therapeutic action of the sulfones, its use is deemed advisable in lepromatous patients not only in the treatment of lepra reaction but also during the rest period of sulfone therapy.

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18. Romero, A., and Brenes Ibarra, A.: Nota informativa: Estreptomicina en Lepra, Report of the 5th International Congress on Leprosy, Habana, 1948, p. 1286.

19. Romero Jordan, O., and Grau Triana, J.: Resultados obtenidos con la Dihidroestreptomicina en la reacción leprótica, Médica **8**:123, 1949.

20. Erickson, P. T.: Streptomycin: A Useful Adjunct to Sulfone in Certain Leprous Manifestations, America Clinica **14**:123, 1949.

REPORT OF CASES

CASE 1.—*History.*—A. de M., a woman, aged 34, had had lepromatous leprosy since 1941, and had been subject to severe lepra reactions almost continuously without remission since April, 1948. Chaulmoogra oil, sulfones, stibophen, and three blood transfusions had been administered without benefit.

Examination.—On Dec. 13, 1948, the patient was examined and noted to be acutely ill and emaciated, weighing 93 lb. (42 kg.). The daily temperature was elevated to 104 F. and above. Abundant nodular lesions were present, distributed all over the face and body, and there were violaceous infiltrations of the extremities. She also presented evidences of bilateral neuritis of the ulnar, peroneal, and posterior tibial nerves, the early stage of clawhand.

Laboratory Data.—The red blood cell count was 3,400,000 per cubic millimeter; the leucocyte count, 15,000 per cubic millimeter, and the erythrocyte sedimentation rate, 128 mm. in one hour (Westergren). Smears were 3+ positive for Mycobacterium leprae. The reaction to a lepromin test was negative.

Clinical Course.—Under dihydrostreptomycin therapy, 2 gm. per day administered for 20 days, the temperature decreased rapidly, and became normal after three weeks. The patient's appetite and weight gradually improved. The erythrocyte sedimentation rate dropped to 81 mm. per hour, the leucocyte count to 10,000 per cubic millimeter, and the erythrocyte count rose to 4,000,000 per cubic millimeter. The pains subsided, and the skin lesions became paler and less turgid, some undergoing regression. After two weeks a second course of dihydrostreptomycin was given, 2 gm. per day for 10 days. Also, sulfoxone (diasone®) sodium in a dosage of 1 gm. per day, was administered for eight weeks, followed by three weeks of rest, during which 2 gm. per day of dihydrostreptomycin were given for 10 days. This patient has been followed for 25 months during which no relapses have occurred, the skin lesions have regressed, and the neuritic pains have disappeared. Only very few bacilli have been observed in smears.

This case has manifested prompt and remarkable response to the therapy.

CASE 2.—*History.*—P. C., a farmer, aged 48, had had lepromatous leprosy, treated with injections of chaulmoogra oil, since 1940. In 1947, he suffered from three lepra reactions of moderate severity. Diphtheria toxoid and sulfones were included among various methods of therapy employed. There were two relapses in 1948, and when the patient was seen on April 20, 1949, the lepra reaction had been present for four weeks.

Examination.—The patient presented extensive lepromatous infiltrations of the face, arms, dorsa of the hands, trunk, and lower extremities, which involved the skin almost completely. Bilateral extremely painful ulnar neuritis, fibrous orchitis, gynecomastia, iridocyclitis of the right eye, recent ulceration of the nasal septum, and arthralgia were also present. The temperature was 102.2 to 104 F.

Laboratory Data.—The erythrocyte sedimentation rate was 110 mm. in one hour (Westergren). Smears were 3+ positive for Mycobacterium leprae; the reaction to the lepromin test was negative. The red blood cell count was 3,700,000 and the leucocyte count 12,000 per cubic millimeter.

Clinical Course.—Dihydrostreptomycin was administered in a dosage of 2 gm. daily for three weeks, resulting in healing of the nasal ulceration, drop in temperature, and improvement of the ocular condition and of the constitutional disturbances. After a rest of three weeks, a second course of dihydrostreptomycin was given for another two weeks. Sulfoxone sodium was then administered, and during the rest periods of this therapy dihydrostreptomycin was given in 10-day courses to enhance the sulfone effect.

No relapses have occurred since the patient's last reaction in April, 1949. The lepromatous infiltrations have been reabsorbed, the smears are only 1+ positive for bacilli, and the sedimentation rate is down to 70 mm. in one hour.

The clinical result in this patient is considered excellent, the improvement having begun promptly with dihydrostreptomycin therapy and been well maintained.

CASE 3.—*History.*—E. V., a 14-year-old girl, who had had a mildly lepromatous condition for four years, presented the clinical picture of acute onset of fever (temperature 100.4 to 102.2 F.) accompanied with prostration, headache, and generalized pains. The symptoms had become aggravated after the administration of sulfoxone sodium.

Examination.—Upon examination on June 9, 1949, it was noted that the nodules on the dorsum of the right hand had become confluent and necrotic, producing an ulcer the size of a half dollar, which was associated with marked edema and pain. The nodules on the ears, however, although tense and inflamed, had not broken down.

Laboratory Data.—The red blood cell count was 3,700,000 per cubic millimeter, and the leucocytes, 12,200 per cubic millimeter; hemoglobin was 70%, and the erythrocyte sedimentation rate was 108 mm. in one hour (Westergren). Smears of skin lesions were 3+ positive for lepra bacilli.

Clinical Course.—After one week of treatment with dihydrostreptomycin, 2 gm. daily, there was a fall in the temperature and amelioration of the constitutional symptoms. The edema of the hand regressed. By the end of the third week of treatment, the ulcer was healed. A second course of treatment was begun two weeks later and continued for 10 days. Repeat laboratory tests revealed the red blood cell count to be 4,000,000 per cubic millimeter, the white blood cell count, 9,100 per cubic millimeter, and hemoglobin 75%. Smears, however, were still 3+ positive for bacilli.

Treatment with sulfoxone sodium was then begun and was well tolerated. Fifteen months after the beginning of treatment all skin lesions had disappeared and smears were now negative for bacilli. In addition, the patient had gained 12 lb. (5.4 kg.).

The clinical response to dihydrostreptomycin therapy in this case was rapid and excellent.

CASE 4.—*History.*—E. P., a farmer, aged 37, had a disease which began in September, 1949, with an acute episode of fever, weakness, arthralgias, anemia, and loss of weight. These manifestations were considered to be rheumatic in nature and were treated as such.

Examination.—When examined on Dec. 10, 1949, he had a temperature of 101.3 to 102.2 F., and weighed 124 lb. (56 kg.). He presented lepromatous infiltrations of both ears and over the eyebrows and cheeks and discrete lepromas in the buttocks and limbs. Erythema nodosum lesions were abundantly present on the chest, arms, and thighs. There was also bilateral ulnar neuritis, with flattening of the thenar and hypothenar eminences.

Laboratory Data.—The erythrocyte sedimentation rate was 95 mm. in one hour; the erythrocyte count was 3,700,000 per cubic millimeter; leucocyte count, 10,600 per cubic millimeter, and hemoglobin, 70%. The reaction to the lepromin test was negative. Skin smears were 2+ positive for lepra bacilli.

Clinical Course.—The patient received dihydrostreptomycin in a dosage of 2 gm. per day for three weeks. After 10 days the fever abated, and the temperature became normal. There was also marked general improvement, with flattening of the lepromas and regression of the erythema nodosum lesions. The Westergren erythrosedimentation rate was reduced to 70 mm. in one hour. Following a rest of two weeks, a second course of dihydrostreptomycin was given over a period of two weeks. The patient gained 7 lb. (3.2 kg.). Sulfoxone sodium therapy was then begun and was maintained for eight weeks. On Sept. 20, 1950, the patient returned from the country with a relapse that lasted three weeks. Despite the continuation of dihydrostreptomycin, relapses occurred every three or four months until Jan. 12, 1951, when he was last seen. At this time, the lepromas were noted to have partially regressed, but erythema lesions were present, and there were diffuse infiltrations in the skin of the thighs. The temperature was elevated to 100.4 to 102.2 F., and the patient complained of severe pains in both lower extremities.

In this case, although the early therapeutic response was good, a relapse occurred after nine months and again three months later.

CASE 5.—*History.*—E. P., a housewife, aged 31, was vaccinated against smallpox in February, 1949. Two weeks later, eruptive lesions developed, with constitutional symptoms consisting of fever, headache, and muscular pains. These manifestations subsided for a few weeks but then relapsed. She was seen on Jan. 15, 1950, at which time she had had a moderate lepra reaction of two weeks' duration. Her temperature was 101.3 F.

Examination.—Examination revealed the presence of isolated nodules on the forehead, ears, chest, and upper extremities, and associated lesions of erythema multiforme and erythema nodosum. In addition, there were violaceous deep infiltrations in the thighs and signs of right ulnar neuritis.

Laboratory Data.—A blood count showed hemoglobin to be 65%; erythrocytes, 4,100,000 per cubic millimeter, and leucocytes, 9,000 per cubic millimeter. The erythrocyte sedimentation rate was 85 mm. in one hour. Smears were 2+ positive for acid-fast bacilli. The reaction to the lepromin test was negative.

Clinical Course.—Therapy consisted of 2 gm. of dihydrostreptomycin daily for 15 days, with which gradual regression of the skin lesions and definite clinical improvement were observed, with defervescence and reduction in the sedimentation rate to 60 mm. After a rest of two weeks, the patient received a second course of dihydrostreptomycin for two weeks, and sulfone therapy was then instituted.

In early September, 1950, the patient again had a low-grade fever, and she presented discrete erythema nodosum lesions. These regressed after cessation of the sulfone therapy and the administration for two weeks of dihydrostreptomycin in doses of 2 gm. daily.

A slight relapse occurred seven months later. However, this was rapidly checked, and no further relapses have occurred since then.

CASE 6.—*History.*—X. L., a housewife, aged 37, was first examined in June, 1933, when her condition was diagnosed as "undifferentiated type of leprosy." Chaulmoogra oil injections were prescribed, but these were discontinued after a few months because of regression of the cutaneous manifestations. In March, 1949, the patient became suddenly ill. She suffered three slight lepra reactions and was treated with penicillin and sulfone, but these had to be discontinued because of aggravation of the condition. When seen on April 7, 1950, sixteen years after the onset of the disease, the patient's last lepra reaction was of four weeks' duration.

Examination.—The patient was weak and prostrated, her temperature was 102.4 F., and she presented dull-red, painful nodules and edematous infiltrations on the face, upper extremities, and hands. The skin of the lower extremities was thick, deeply infiltrated, and pigmented. In addition, inguinocrural lymphadenitis was present.

Laboratory Data.—The blood count showed hemoglobin to be 65%; red blood cells, 4,100,000 and white blood cells, 10,000. The erythrocyte sedimentation rate was 95 mm. in one hour. The reaction to the lepromin test was negative. Smears were 3+ positive for acid-fast bacilli.

Clinical Course.—Dihydrostreptomycin, in a dosage of 2 gm. daily, was given for three weeks. Clinical improvement was noted in the patient after one week of treatment, as evidenced by normal temperature, regression of the nodules and infiltrations, and the patient feeling stronger. A second three weeks' course of the dihydrostreptomycin was begun two weeks after the termination of the first, after which the hemoglobin was 70%, the erythrocyte count, 4,200,000 per cubic millimeter, the leucocyte count, 7,500 per cubic millimeter, and the sedimentation rate, 60 mm. in one hour. Acid-fast bacilli were less numerous in the smears.

Sulfoxone sodium therapy was then instituted and well tolerated. After nine months, there have been no relapses, the lymphadenitis and skin lesions have regressed, and the smears show but few acid-fast bacilli.

CASE 7.—*History.*—A. A., a 30-year-old man, had had a succession of rather severe lepra reactions since September, 1949. When examined on May 9, 1950, he presented many new nodules on the trunk and on the extremities, lepromatous infiltrations of the face, signs of bilateral ulnar neuritis, and pronounced swelling of the hands associated with severe pains. His temperature varied between 102.2 F. and 104 F. He had been treated with sulfoxone sodium, but this had not been well tolerated.

Laboratory Data.—The blood count was as follows: hemoglobin, 62%; red blood cells, 3,700,000 per cubic millimeter, and white blood cells, 16,800 per cubic millimeter. The erythrocyte sedimentation rate was 102 mm. in one hour (Westergren). The reaction to the lepromin test was negative; smears were 3+ positive for bacilli.

Clinical Course.—The patient received dihydrostreptomycin in a dosage of 2 gm. per day for three weeks with no clinical improvement. A similar course of treatment, begun two weeks later, also failed to influence the symptoms, and the laboratory findings remained unaltered as well.

This patient exhibited no response to dihydrostreptomycin therapy.

CASE 8.—*History.*—M. C., a woman, 30 years old, a school teacher, had suffered from mild lepromatous leprosy for three years, exhibiting partially involuted lepromas on the ears, eye-

brows, and hands. Coincident with sulfoxone sodium therapy, severe neuritis of the large nerve trunks developed, with extensive and thick infiltrations of the skin of the extremities, some of which became ulcerated. Fever was low-grade. When examined on June 8, 1950, she complained of extremely painful neuritis which impeded her walking.

Laboratory Data.—The blood count showed hemoglobin to be 65%; erythrocytes, 3,900,000 per cubic millimeter, and leucocytes, 12,000 per cubic millimeter. Smears were 2+ positive for bacilli. The reaction to the lepromin test was negative. The erythrocyte sedimentation rate was 80 mm. in one hour (Westergren).

Clinical Course.—Dihydrostreptomycin was administered in doses of 2 gm. per day for three weeks. After six days of therapy, the temperature became normal and the patient's pain decreased rapidly. The ulcers of the limbs were healed at the end of the third week; also, the infiltrations became less turgid, some of them undergoing regression.

A second two weeks' course of dihydrostreptomycin, in similar dosage, was begun after a rest interval of two weeks; then, following three weeks of rest, a third course was given for three more weeks.

The patient exhibited marked constitutional improvement. The sedimentation rate decreased to 40 mm. in one hour, but the smears remained 2+ positive for bacilli. Sulfoxone sodium therapy was then resumed and was well tolerated. No clinical relapses have occurred.

This case manifested a prompt and satisfactory therapeutic response, with immediate relief of neuritic pain and healing of the ulcerations.

CASE 9.—*History.*—E. C. de A., a 31-year-old woman, had suffered from a moderate lepromatous leprosy since August, 1946. In June, 1949, she was treated with glucosulfone (promin®) sodium for six weeks, but this was discontinued by the patient because of the intercurrent complication of a herpes zoster intercostalis.

Examination.—The patient was seen three weeks after the onset of a mild lepra reaction. At this time, her temperature was 101.3 F., and she complained of cephalalgia, anorexia, and weakness. There were a few lepromas on the face and hands, with a tense, infiltrated plaque on the forehead. In addition, she presented perforating ulcers on the soles of the feet and signs of a moderate left ulnar neuritis.

Laboratory Data.—The blood count was as follows: hemoglobin, 70%; red blood cells, 4,030,000 per cubic millimeter, and white blood cells, 11,500 per cubic millimeter. The erythrosedimentation rate was 70 mm. in one hour. The reaction to the lepromin test was negative, and smears contained a moderate number of acid-fast bacilli.

Clinical Course.—Dihydrostreptomycin was administered in a dosage of 2 gm. daily for three weeks. The temperature fell, there was improvement in the constitutional symptoms, the ulcer healed, and the neuritic pains subsided. Also, the infiltrated plaque on the face became flattened, and the lepromatous nodules underwent partial involution.

After a two-week resting interval, a second and then a third course of dihydrostreptomycin, each of three weeks' duration, were given. The sedimentation rate was now 20 mm. However, the number of bacilli seen on smears remained unaltered.

Although sulfone therapy was refused, the beneficial results obtained with dihydrostreptomycin in this case have been maintained. The patient was last observed on Jan. 15, 1951; there had been no relapses.

SUMMARY

On the basis of the small number of cases herein reported, definite conclusions should not be drawn regarding the efficacy of inhibitory action of dihydrostreptomycin upon the Mycobacterium leprae. No benefit was observed in one patient, and in another, although there was a remission of symptoms and clinical improvement as indicated by laboratory tests, the occurrence of a relapse was not prevented. The latter, however, was checked by further administration of the antibiotic.

In the remaining patients in this series, on the other hand, abatement of painful neuritis and healing of perforating ulcerations of the soles of the feet, nasal septum, and other parts of the body were observed. Defervescence of pyrexia, gain in weight, amelioration and disappearance of constitutional symptoms, and modification of some of the laboratory findings were also achieved.

The clinical experience in these cases seems to indicate that the two most actively efficacious agents in the therapy of leprosy are the sulfones and streptomycin, or its less toxic related compound, dihydrostreptomycin. During acute reactions, when sulfones have effected no improvement or have had to be discontinued, dihydrostreptomycin has proved to be an excellent therapeutic agent. I feel, therefore, that dihydrostreptomycin constitutes the best therapeutic agent for lepra reaction in use at this time. Administered during the resting periods of the sulfone therapy, it is a valuable adjunct in the treatment of lepromatous leprosy.

However, further clinical investigations along these lines will be required in order to determine the real value of this drug in the control of lepra reaction as well as in the therapy of leprosy.

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ABSTRACT OF DISCUSSION

Dr. M. T. Van Studdiford, New Orleans: The observation made at the United States Marine Hospital at Carville, La., on 114 patients treated with streptomycin and dihydrostreptomycin indicates that antibiotics are effective agents for the treatment of leprosy. With certain limitations they appear to be on a par with the sulfones and often act even more rapidly in effecting regressive changes. In combination with the sulfones they hasten resolution of the lesion, and they can be administered without difficulty for short periods of time when the dosage of sulfones must be reduced or discontinued because of the onset of anemia or erythema nodosum.

In patients in whom the disease has reached a stationary stage, administration of streptomycin or dihydrostreptomycin, either in addition to sulfones or alone, is shortly followed by renewed clearing of residual lesions, and rapid healing of resistant nasal and laryngeal mucous membrane lesions is accomplished. Attacks of acute leprous iridocyclitis which are independent of generalized lepra reactions are usually aborted with relief of the intense discomfort. Because of the toxic properties peculiar to both streptomycin and dihydrostreptomycin and because of the effect on the eighth cranial nerve, which usually appears after three to six months of therapy, the usefulness of these drugs is limited. However, lepra reactions are reduced in frequency by streptomycin and dihydrostreptomycin treatment as with the sulfones.

The experience at the United States Marine Hospital at Carville has been that these antibiotics seem to be of more value in preventing reactions than in changing the clinical course after the reactions have been precipitated. This would indicate that the causes which underlie the development of lepra reactions are in some way altered by streptomycin and sulfones. The cause of the reaction remains unknown, but experience gained by the use of antibiotics, sulfones, and antihistaminics suggests that the reaction is due to an allergic phenomenon governed by a delicate balance between the lepra bacillus and the body defense mechanism. Muir refers to it as the reaction threshold. The threshold is raised by judicious treatment with streptomycin or sulfone, through a suppressive effect upon the growth of the bacilli, if the growth is not sufficiently depressed by natural processes as therapeutic agents. The reaction threshold is lowered as the disease progresses, and a reaction occurs.

When a reaction occurs in a patient previously treated with the sulfones or streptomycin, the reaction is more likely to respond to streptomycin, since the suppressive effect of the drug on the bacilli has not been already expended.

Dr. Frank C. Combes, New York: I wish to say a few words about the Leonard Wood Memorial (American Leprosy Foundation) and its plans for the immediate future. We had a meeting of the Board of Directors and Advisory Medical Board last fall to which we invited the directors of research of the leading pharmaceutical houses. We propose to set up a research program at various centers throughout the world to test various drugs under varying climatic conditions in the lepromatous types of the disease only. This program will extend over a period of five years. The centers selected are Cebu, P. I.; Hendala, Ceylon; Westfort, Pretoria, Union of South Africa; Chacachacara, Trinidad, W. I., and two undesignated locations in Cuba.

I enjoyed Dr. Saenz' paper very much, as I am always interested in new approaches for the care of this mysterious disease. I feel that streptomycin is much too toxic for routine use,

except for very short periods as an adjunct to sulfoxone sodium or diaminodiphenylsulfone in the leprotic type, or in control of the leprous reaction. Its action can be summarized, I think, under three categories. First, it has a definite effect on secondary infection, which is very important in leprosy; second, it has a definite antileprotic effect of its own, and third, as Dr. Saenz brought out, it acts synergistically with the sulfones, particularly in those patients who do not respond or in whom response is delayed.

There is one more thing I do want to mention. Did you know that it is a federal offense to call a person a leper? You can be prosecuted for it by the Federal Government. That is the reason for the change in name of the American Mission to Lepers to the American Leprosy Mission.

Dr. V. Pardo-Castello, Habana, Cuba: After the introduction of diaminodiphenylsulfone and its derivatives in the therapy of leprosy, lepra reaction, also called leprotic fever, has become rather rare. However, it is still one of the most dreaded complications of the lepromatous type of the disease, one that taxes to the utmost the defensive powers of the patient as well as the therapeutic resources of the physician. Until recently the use of antimony potassium tartrate and of other organic antimony salts by intravenous injection, and in some cases the use of antihistaminics, such as diphenhydramine hydrochloride and tripelennamine hydrochloride, were the only effective means of bringing the lepra reaction under control. These methods are still, in my opinion, quite useful in most cases, together with the general hygienic measures of rest in bed, administration of calcium and blood plasma, and controlled diet. In my experience, increasing the dose of sulfoxone sodium, or diamidine sharply will, in some cases, arrest an incipient attack of lepra reaction.

The use of dihydrostreptomycin is undoubtedly a valuable addition to the therapy, but one wonders whether its action is specific as a bacterial agent against Mycobacterium leprae, since, to the best of my knowledge, this specific action has been disproved in the case of leprosy of the usual chronic type, whether lepromatous or tuberculoid.

Dr. Joseph V. Klauder, Philadelphia: As you know, I am not a leprologist. This is not a discussion of the lepra reaction or its treatment. It concerns, I believe, a new phase in diagnosis of leprosy. The diagnosis of leprosy has been a cutaneous procedure, excepting biopsy of the ulnar nerve to show the organism. This, however, is outmoded. The ocular examination has come into prominence in early diagnosis of leprosy. I refer to what is believed to be a distinctive finding upon slit-lamp examination. This is a beaded appearance of the nerve filaments in the cornea. In a recent examination of a small series of patients in the leprosarium in Nassau in collaboration with an ophthalmologist, 75% of these patients were found to have ocular lesions. We estimated that 10% were in the category of industrially blind.

In leprosy there is a larger percentage and greater incidence of eye involvement than in any other systemic disease. The incidence is as high as 90%. Leprosy is therefore an important cause of blindness. All ocular structures are affected. In addition to its use in early diagnosis by means of slit-lamp examination, the eye is important in the diagnosis of leprosy because the causative organism has been found in corneal scrapings, and, at least in some cases, the organism was present in such scrapings when it was absent in smears obtained from other sources.

Dr. Braulio Sáenz, Habana, Cuba: In seven of the nine cases, the treatment was instituted after the failure of various drugs and other therapeutic methods used in the treatment of severe cases of lepra reaction in lepromatous leprosy. It has been emphasized that encouraging results in the evolution of the process have been observed with the sulfone drugs, the use of which has reduced the incidence of this reaction. Nevertheless, in many cases, the use of sulfone drugs has to be discontinued, as has been mentioned.

One must not interpret the erythema multiforme and erythema nodosum lesions, observed during the use of the sulfones, as indicative of lepra reaction and therefore necessitating discontinuation of the use of these drugs. These lesions represent a beneficial reaction, and I have mentioned that in these patients no serious eye lesions are observed as a complication of the reaction.

The use of antihistaminics in lepra reaction was also mentioned when discussing the pathogenesis and treatment of the reaction. Mom from Buenos Aires was the first, I think, who proposed the use of diphenhydramine hydrochloride to alleviate some manifestations which are accepted as having allergic origin. But to prove conclusively the allergic origin of the reaction, although maintained by some authors, will no doubt take time.

SERUM LIPOPROTEINS AND CHOLESTEROL METABOLISM IN XANTHELASMA

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XANTHELASMA is generally considered to be the commonest external manifestation of essential hypercholesteremic xanthomatosis [1] (familial hypercholesteremia [2]). Major interest in the xanthomatous lesions centers about their importance with respect to the presence or development of atherosclerotic vascular disease. The purpose of this paper is to report observations of 35 patients with xanthelasma, obtained mainly from the private dermatologic practice of one of us (N. N. E.). It was felt of particular importance to study the serum of such patients with respect to lipoproteins which appear to be in some way associated with atherosclerosis.

METHODS

The clinical status of these patients was carefully investigated and was supplemented by electrocardiograms and by the thymol turbidity and sulfobromophthalein (bromsulphalein®) sodium tests of liver function. All patients with nonxanthomatous abnormalities known to be associated with a disturbed cholesterol metabolism were excluded. Particular attention was given to the possible presence of manifest arteriosclerotic cardiovascular disease. Quantitative analysis of the fasting serum cholesterol concentration, together with a standard, was determined according to

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* Research Fellow of the American Heart Association.

Read at the Seventy-First Annual Meeting of the American Dermatological Association, Hot Springs, Va., May 25, 1951.

From the Harold Brunn Institute for Cardiovascular Research; the Department of Dermatology, Mount Zion Hospital, and the Division of Medical Physics, University of California.

1. (*a*) Thannhauser, S. J.: Lipidoses: Diseases of the Cellular Lipid Metabolism, ed. 2, New York, Oxford University Press, 1950. (*b*) Boas, E. P.; Parets, A. D., and Adlersberg, D.: Hereditary Disturbance of Cholesterol Metabolism, Am. Heart J. **35**:611, 1948. (*c*) Adlersberg, D.; Parets, A. D., and Boas, E. P.: Genetics of Atherosclerosis, J. A. M. A. **141**:246 (Sept. 24) 1949. (*d*) Montgomery, H., and Osterberg, A. I.: Xanthomatosis: Correlation of Clinical, Histopathologic and Chemical Studies of Cutaneous Xanthoma, Arch. Dermat. & Syph. **37**:373 (March) 1938.

2. (*a*) Wilkinson, C. F., Jr.; Band, E. A., and Fliegelman, M. J.: Essential Familial Hypercholesterolemia, Ann. Int. Med. **29**:671, 1948. (*b*) Boas, E. P., and Adlersberg, D.: Familial Hypercholesterolemia (Xanthomatosis and Atherosclerosis), J. Mt. Sinai Hosp. **12**:84, 1945.

the method of Saifer and Kammerer[3] as previously modified.[4] "Qualitative" analysis of the serum cholesterol was obtained according to the method of Gofman and his associates.[5]

CLINICAL FINDINGS

The important positive clinical findings are presented in Table 1 and summarized in Table 2. The 35 patients comprising this study included 12 men and 23 women.

3. Saifer, A., and Kammerer, O. F.: Photometric Determination of Total Cholesterol in Plasma or Serum by Modified Liebermann-Burchard Reaction, J. Biol. Chem. **164**:657, 1946.

4. Byers, S. O., and Friedman, M.: Hypercholesteremia in the Rat After Intravenous Administration of Cholesterol, J. Biol. Chem. **177**:841, 1949.

5. The various lipids of serum, including cholesterol and its esters, phospholipids, and neutral fats (glycerol esters), exist in the blood in the form of giant molecular complexes with one another, and with more or less protein, depending upon the particular giant molecule in question. These complex molecules appear to fall into certain definite categories, such that the findings on a single person are reproducible from time to time, and such that differences in blood pattern of lipid transport from person to person can be detected and measured quantitatively. The procedure found most useful for this purpose is analytic ultracentrifugation.

With this technique it has been possible to discern and describe several different types of giant lipoproteins in blood. Since no better term has yet suggested itself for the various molecular species, they have been named by their rates of flotation under specified conditions in the ultracentrifuge. These rates are described in S_f values (signifying Svedberg units of flotation).

Under the conditions specified by Gofman and his co-workers, the lipoproteins in human sera (of the low density class) are the S_f 4, S_f 6, S_f 8, S_f 10, S_f 13, and S_f 17 molecules. Above these there is a series of closed spaced components from S_f 17 to greater than S_f 500. All of these species represent cholesterol and lipid-bearing lipoproteins. With respect to atherosclerosis or any other pathologic process, one wants to know whether any of such molecules, certain of these molecules, or all of these molecules are in any way related to extent or rate of development of disease. Unfortunately, in the present state of progress an unequivocal answer cannot be given to this question. However, studies to date have revealed that certain of the lipoproteins may bear a higher degree of relationship to development of atherosclerosis than do others. For example, it has been possible to show that the concentration of lipoproteins with S_f rates between 10 and 20 is elevated, in general, in patients with angina pectoris or myocardial infarction, these two states serving as indicators for the presence of atherosclerosis. Further, it appears that the presence of high concentrations of lipoproteins in the S_f 10-to-20 class may be a manifestation of a metabolic defect of varying degrees of severity. All persons from infancy onwards show some lipoprotein in the S_f 4-to-S_f 6 class. However, of the group of lipoproteins listed above (i. e., from S_f 8 to S_f 500) some persons do and others do not show significant concentrations in the serum. For the region between S_f 8 and S_f 20 (and possibly up to S_f 30), the sequence of types of manifestations of the defect is as follows, in order of increasing severity:

(*a*) S_f 8 alone may be present in addition to the molecules of the S_f 4-to-6 class.

(*b*) S_f 10 may be present, but only if S_f 8 is already present.

(*c*) S_f 13 may be present, but only if S_f 8 and S_f 10 are present.

(*d*) S_f 17 may be present, but only if S_f 8, 10, and 13 are present.

(*e*) S_f 17 to 30 may be present, but only if S_f 8, 10, 13, and 17 are present.

In general, as the serum cholesterol concentration rises, there is an increasing likelihood of finding appreciable levels of the molecules from S_f 8 to S_f 30, but this is an imperfect correlation, since many persons show low serum cholesterol levels but high S_f 8-to-30 levels, whereas others with high cholesterol levels show low S_f 8-to-30 levels, or may show S_f 8 without the higher numbers. (Gofman, J. W.: The Role of Lipids and Lipoproteins in Atherosclerosis, Science **111**:166, 1950. Gofman, J. W.; Jones, H. B.; Lindgren, F. T.; Lyon, L. P.; Elliott, H. A., and Strisower, B.: Blood Lipids and Human Atherosclerosis, Circulation **2**:161, 1950.)

TABLE 1.—*Positive Findings in Thirty-Five Patients with Xanthelasma*

Patient No.	Age	Sex	Duration, Yr.	Myocardial Infarction	Angina Pectoris	Congestive Heart Failure	Arteriosclerotic Peripheral Vascular Disease	Arteriosclerotic Cerebrovascular Disease	Arterial Hypertension; Blood Pressure	Cholelithiasis	Obesity	Dietary Fat Intake†	Abnormal ECG	Family History*: Xanthelasma	Family History*: Coronary Artery Disease	Family History*: Cerebrovascular Disease	Family History*: Cholelithiasis	Serum Cholesterol Concentration: Total, Mg. per 100 Cc.	Serum Cholesterol Concentration: Cholesterol Esters, Mg. per 100 Cc.	Serum Cholesterol Concentration: Lipoprotein Sr 10-20 units, Mg. per 100 Cc.
1	49	F	1½	..	..	..	..	..	.....	..	..	1	..	..	1	1	..	330	69	48
2‡	46	F	1	..	..	..	..	..	.....	..	..	3	..	..	..	..	..	310	81	31
3	47	M	½	+	+	+	..	..	+	..	..	2	+	1	..	1	1	391	71	45
4§	41	F	20	..	..	..	..	..	.....	..	+	2	..	2	..	..	..	357	76	..
5§	70	F	40	..	..	..	..	..	.....	..	..	2	..	2	..	..	..	287	72	33
6	61	F	5	..	..	..	..	..	.....	+	+	2	..	..	..	..	..	371	77	152
7‖	61	M	2	..	..	..	+	..	.....	..	+	2	..	1	..	..	..	261	74	103
8	48	F	10	..	..	..	..	..	.....	..	..	2	..	4	1	..	..	233	74	36
9	68	M	20	+	+	+	..	..	190/92	..	+	3	+	1	1	..	..	319	78	50
10	58	M	30	..	..	..	..	..	180/96	..	+	2	..	..	1	..	..	360	78	37
11	46	M	15	..	..	..	..	..	.....	..	..	2	..	..	..	..	..	331	79	64
12	47	F	5	..	..	..	..	..	.....	..	..	1	..	..	..	..	..	238	81	26
13	57	F	15	..	..	..	..	..	.....	..	+	2	..	..	..	..	..	272	77	22
14‡	52	F	1	..	..	..	..	..	.....	?	..	2	+	..	..	..	..	283	79	53
15‡	69	F	20	..	+	+	..	..	160/100	..	..	1	+	2	4	..	..	375	82	24
16	53	M	3	..	..	..	..	..	.....	..	..	2	..	..	..	1	..	242	78	24
17	63	F	25	..	..	..	..	..	170/90	+	+	2	..	..	..	..	..	287	79	44
18	41	F	5	..	..	..	..	..	.....	..	..	2	..	..	..	..	..	232	86	20
19	37	F	1	..	..	..	..	..	.....	..	+	2	..	..	1	..	..	294	69	24
20	54	F	5	..	..	..	..	..	.....	..	+	1	..	1	1	..	..	252	78	11
21	54	F	25	+	+	..	..	+	200/120	..	+	3	+	..	2	1	1	352	70	55
22	48	F	15	..	..	..	..	..	.....	..	+	2	..	1	1	..	..	228	73	46
23	63	F	15	..	..	..	..	..	170/100	..	..	1	+	..	..	..	..	304	48	7
24¶	54	F	15	..	..	..	..	..	.....	..	..	2	..	2	..	..	..	277	61	..
25¶	24	F	½	..	..	..	..	..	.....	..	..	2	..	2	..	..	..	314	75	15
26	37	M	3	..	..	..	..	..	.....	..	+	2	+	2	1	..	1	426	70	84
27	70	F	15	..	+	..	..	..	220/130	..	..	2	+	..	..	..	..	345	53	75
28	46	M	5	..	..	..	..	..	.....	..	..	2	+	2	..	1	..	281	77	31
29	59	M	5	+	..	..	..	..	.....	..	..	2	+	..	2	..	..	220	78	26
30	61	M	10	..	..	..	..	..	200/130	..	+	2	+	..	..	..	..	....	..	64
31‡	31	M	5	..	..	..	..	..	.....	..	+	3	..	2	..	..	1	246	86	47
32	53	F	10	..	..	..	..	..	180/110	..	+	2	+	..	..	..	..	255	79	32
33	41	M	8	..	..	..	..	..	.....	..	+	2	..	1	..	..	..	340	85	60
34	48	F	15	..	..	..	..	..	.....	+	+	2	..	..	..	..	4	246	80	..
35	48	F	15	..	..	..	..	..	.....	..	+	2	..	..	..	..	..	305	78	22

* Number of immediate family having history of abnormality, i. e., parents, grandparents, siblings, aunt or uncle.
† Low, 1; average, 2; high, 3.
‡ Patients 2 and 31 had recurrent peptic ulcers.
§ Patient 4 is the daughter of Patient 5.
‖ Patient 7 had arteriosclerotic heart disease; Patient 14, rheumatic heart disease; Patient 15, syphilitic heart disease.
¶ Patient 24 is the niece of Patient 25.

TABLE 2.—*Summary of Pertinent Findings in Thirty-Five Patients with Xanthelasma*

	No. of Cases	Per Cent
Atherosclerotic cardiovascular disease	7	20.0
Arterial hypertension	10	28.6
Cholelithiasis	4	11.4
Obesity	18	51.4
Family history		
Xanthelasma	15	42.9
Coronary artery disease	11	31.4
Cerebrovascular disease	5	14.3
Cholelithiasis	5	14.3
Total serum cholesterol concentration		
Greater than 221 mg. per 100 cc	34	100.0
Greater than 300 mg. per 100 cc	16	47.0

Tendon or cutaneous xanthoma, other than xanthelasma, were not present in any patient. The majority of the patients were in the age group 40 to 63 years. The known duration of the xanthelasma varied from less than 1 year to more than 30 years. Obesity was present in 18 patients, but this was minimal in 4. The family history, of little significance statistically, revealed a familial occurrence of xanthelasma in 15 instances, but a history of other xanthoma was not obtained. The thymol turbidity and sulfobromophthalein sodium tests of liver function were within normal limits in the patients included in the study.

Coronary artery disease was apparent in at least six and probably seven patients (20%). Myocardial infarction had occurred in four patients, and angina pectoris was present in two others. Patient 21 presented evidence of previous cerebrovascular accidents. Arterial hypertension was found in 10 patients, but in only 6 of these was the diastolic pressure abnormally elevated. In the other four instances, only a systolic elevation was present, possibly related to arteriosclerosis of the aorta. The electrocardiogram was abnormal in 12 patients. The abnormalities were clearly related to the presence of coronary artery disease in six instances, and in four, to left ventricular hypertrophy associated with arterial hypertension (Patients 23, 30, and 32) or with aortic insufficiency (Patient 14). There were two patients (Nos. 26 and 28) in whom the electrocardiograms were abnormal, although no evidence of organic cardiovascular disease was observed.

Coronary artery disease was known in the families of at least 11 patients. It is significant that a brother of Patient 15 died of myocardial infarction at the age of 21, and a brother of Patient 26 died at the age of 39 after many years of angina pectoris. Arteriosclerotic cerebrovascular disease was present in the families of at least five patients.

RESULTS OF SERUM CHOLESTEROL ANALYSES

The total serum cholesterol concentration was greater than 220 mg. per 100 cc. in every patient and exceeded 300 mg. per 100 cc. in 16 patients (47%). The percentage of cholesterol esters was normal in all but nine patients. It was greater than 82% in three patients and less than 66% in two others. In a group of ostensibly normal controls, aged 20 to 75, the total serum cholesterol concentration rarely exceeded 300 mg. per 100 cc. On the basis of the results of the control values obtained for this and other studies, a serum cholesterol concentration greater than 300 mg. per 100 cc. is considered abnormal.

In the 35 patients with xanthelasma, the total serum cholesterol concentration often exceeded 300 mg. per 100 cc., yet for the over-all group of levels of S_f 10-to-20 molecules (excluding S_f 10 itself) show essentially the same distribution of high and low S_f 10-to-20 levels as would be found in an equivalent sample of the general population (Chart 1). Thus, there is an apparent dissociation between the two types of findings. That segment of the xanthelasma group showing hypertension and coronary artery disease appears to have S_f 10-to-20 levels above the rest of the group, although this particular series is too small to be definitive (Chart 2).

No relation could be established between the serum cholesterol concentration and the dietary intake of fat and cholesterol, the presence of obesity, or the family history.

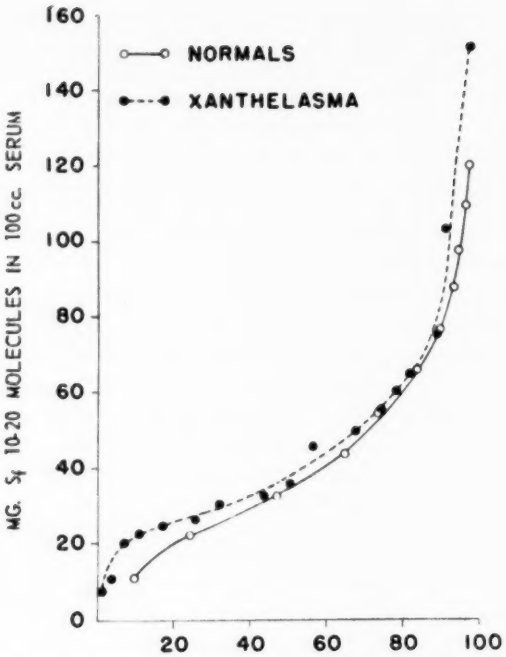

Chart 1.—Per cent of xanthelasma patients, men and women, aged 41 to 70 only, compared with normal persons with S_f 10-to-20 molecule concentration less than any given level.

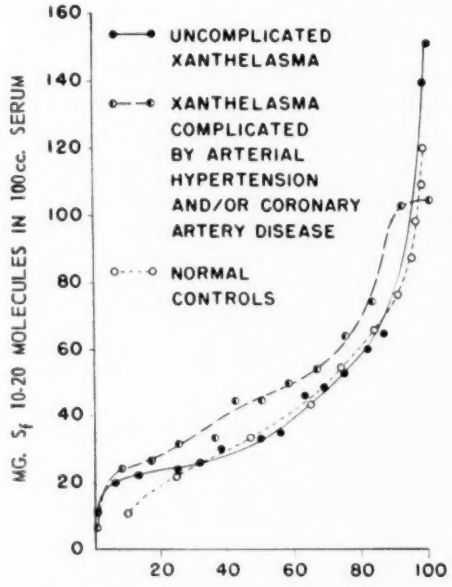

Chart 2.—Per cent of patients, men and women, aged 41 to 70 only, with uncomplicated xanthelasma with S_f 10-to-20 molecule concentration less than any given level; comparison with normal controls and patients with xanthelasma complicated by hypertension and/or coronary artery disease.

COMMENT

The considerable confusion which for many years surrounded the various lipidoses was greatly clarified by the studies of Montgomery[6] and Thannhauser,[7] although the mechanism of xanthoma formation is still not fully explained.[8]

Essential hypercholesteremic xanthomatosis is a familial disorder in which are involved, alone or together, flat and tuberous xanthoma of the skin and tendons and xanthoma of blood vessels, endocardium, and, rarely, the lining of the larger bile ducts.[1a] The lesions are composed of "xanthoma cells" in a fibromatous tissue with Touton giant cells and a prevalence of fibroblasts, but with an absence of granulomatous reaction. Because xanthelasma has a histologic pattern similar to that of flat and nodular cutaneous xanthoma, and because the two alternate in family trees,[9] xanthelasma is generally considered to be an external manifestation of the same process.[10]

It has become apparent that the various characteristics of this syndrome are present simultaneously only rarely,[11] the different features usually alternating in the members of involved families.[12] Xanthelasma is the commonest of the cutaneous xanthoma in such families.[1] In many members only hypercholesteremia may be present,[13] and this has been termed the partial form or forme fruste of this syndrome.[1a] There is no convincing evidence, however, that all persons with an apparently idiopathic hypercholesteremia are manifesting the forme fruste type of this syndrome.[14]

The blood serum is transparent and the neutral fat content usually normal.[1a] The serum phospholipid concentration may be normal,[1a] but is often elevated.[15] The percentage of cholesterol esters is usually normal,[16] but it may occasionally be

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6. (*a*) Montgomery, H.: Xanthomatosis: Cutaneous Xanthoma, Especially in Relation to Diseases of Liver, J. Invest. Dermat. **1**:325, 1938; (*b*) Xanthomatosis: A Systemic Disease, Proc. Staff Meet., Mayo Clin. **12**:641, 1937; (*c*) Cutaneous Xanthomatosis, Ann. Int. Med. **13**:671, 1939; (*d*) Cutaneous Manifestations of Diseases of Lipoid Metabolism, M. Clin. North America **24**:1249, 1940. (*e*) Montgomery and Osterberg.[1d]

7. Thannhauser.[1a] Thannhauser, S. J., and Magendantz, H.: The Different Clinical Groups of Xanthomatous Diseases: A Clinical Study of 22 Cases, Ann. Int. Med. **11**:1662, 1938. Thannhauser, S. J.: Cholesterol Metabolism and the Different Groups of Xanthomatous Diseases, Proc. California Acad. Med., 1937-1938, p. 97.

8. (*a*) Footnote 1*a* and *d*. (*b*) Sperry, W. M.: The Biochemistry of the Lipoidoses, J. Mt. Sinai Hosp. **9**:799, 1942.

9. (*a*) Footnote 1*a* and *d*. (*b*) Müller, C.: Angina Pectoris in Hereditary Xanthomatosis, Arch. Int. Med. **64**:675 (Oct.) 1939; also Acta med scandinav. supp. 89, p. 75, 1938.

10. Footnote 1. Footnote 2*b*.

11. (*a*) Footnotes 1*a* and 2*a*. (*b*) Fliegelman, M. T.; Wilkinson, C. F., and Band, E. A.: Genetics of Xanthoma Tuberosum Multiplex, Arch. Dermat. & Syph. **58**:409 (Oct.) 1948.

12. Thannhauser.[1a] Adlersberg, Parets, and Boas.[1c] Müller.[9b] Fliegelman, Wilkinson, and Band.[11b]

13. Adlersberg, Parets, and Boas.[1c] Müller.[9b] Fliegelman, Wilkinson, and Band.[11b]

14. Footnote 1*a*, *b* and *c*.

15. (*a*) Footnotes 6*d* and 1*d*. (*b*) Curtis, A. C., and Berger, J. P.: Effect of Feeding a Liprotic Substance to Patients with Xanthelasma, Arch. Dermat. & Syph. **52**:252 (Oct.) 1945.

16. (*a*) Footnotes 1*a*, 6*c* and *d*. (*b*) Wilkinson, C. F.: Blecha, E., and Reimer, A.: Is There a Relation Between Diet and Blood Cholesterol? Arch. Int. Med. **85**:389 (March) 1950. (*c*) Sperry, W. M., and Schick, B.: Essential Xanthomatosis: Treatment with Cholesterol-Free Diet in 2 Cases, Am. J. Dis. Child. **51**:1372 (June) 1936.

elevated,[17] as was noted in several instances in this study. Hypercholesteremia is usually present in cases of xanthoma tuberosum [18] but has been noted in a lower incidence in patients manifesting only xanthelasma.[19] Furthermore, the serum cholesterol elevations are of less magnitude in xanthelasma than in xanthoma tuberosum.[20] Thus, various studies of patients with xanthelasma have revealed hypercholesteremia in 40 to 70% of the patients.[21] Although usually of moderate degree, definite hypercholesteremia was found in 47% of the patients studied by us. It is significant, moreover, that the remaining patients had serum cholesterol concentrations in the upper part of the normal range.

Although Müller found no relation between the cholesterol level and the presence of cardiovascular disease,[9b] extensive studies of involved families have shown that the latter occurs but rarely in the absence of hypercholesteremia.[11b] Nevertheless, on occasion, coronary artery disease has been observed in patients with xanthelasma in the absence of hypercholesteremia,[22] a situation found in two instances in this study. Although hypercholesteremia may be observed commonly in the members of such a kindred, the cutaneous and cardiovascular lesions occur much less frequently.[22] An intensive form of arteriosclerotic cardiovascular disease frequently occurs at an early age in persons with xanthoma tuberosum or/and tendinosum.[23] In patients with only xanthelasma, cardiovascular disease occurs less commonly,[24] although the incidence of the latter is still significant.[25] In general, hypercholesteremia has been found in about one-half and cardiovascular disease in about one-fourth the patients with xanthelasma,[21b] figures which are similar to those of this study. It is significant to recognize that coronary artery disease and even myocardial infarction may occur at very early ages in the members of afflicted families [26] and even in the absence of cutaneous xanthoma.[27] Although it has been claimed that the vascular lesions differ in certain respects from those found in the ordinary type of arteriosclerosis,[1a] most observers have not been able to distinguish them.[28] Arterial hypertension was present in this series more commonly than has been previously noted.[29]

Several xanthelasma patients with elevated total serum cholesterol concentrations had low or moderate levels of S_f 10-to-20 molecules. In evaluation of athero-

17. Thannhauser.[1a] Sperry and Schick.[16e]

18. Footnote 1*a*, *b*, and *c*. Footnote 8*c*.

19. Thannhauser.[1a] Montgomery.[6c] Müller.[9b]

20. Thannhauser.[1a] Montgomery.[6c] Montgomery and Osterberg.[1d] Müller.[9b]

21. (*a*) Footnotes 6*c* and *d*, and 15*b*. (*b*) Montgomery, H., in discussion on Wilkinson.[16b]

22. Footnote 1*b* and *c*. Footnote 16*c*.

23. Footnote 1*a*, *b*, and *c*. Footnote 6*d*. Footnote 9*b*. Footnote 21*b*.

24. Footnote 6*c* and *d*. Footnote 1*d*.

25. Footnote 1*b* and *c*.

26. Montgomery.[6d] Müller.[9c] Rigdon, R. H., and Willeford, G.: Sudden Death During Childhood with Xanthoma Tuberosum, J. A. M. A. **142**:1268 (April 22) 1950. McKinney, P. P.: Xanthoma Palpebrarum and Cardiovascular Disease, Brit. M. J. **2**:1259, 1950.

27. Footnotes 1*b*, *c*, and *d*.

28. Müller.[9b] Walin, C.: Coronary Artery Sclerosis as Symptom of Xanthomatosis, Acta med. scandinav. **134**:53, 1949.

29. Footnote 1*a* and *b*. Footnote 9*b*.

sclerogenic potentialities in these cases, the elevated serum cholesterol would bespeak an increase in such potentialities; the S_f 10-to-20 levels would not. A final answer can come only through the long-term follow-up of precisely such a group, i. e., a group with "normal" S_f 10-to-20 levels, but with elevated total serum cholesterol concentrations. However, certain of the apparent discrepancies may be explainable now. First, from the general pattern of appearance of molecules of the S_f 8-to-30 class, it appears that there must usually be a certain level of build-up of the S_f 4-to-6 class, though exceptions exist. The xanthelasma patients with high total cholesterol concentrations but low S_f 10-to-20 levels do manifest high S_f 6 levels, and some show high S_f 8 levels, too. These patients may be in an intermediate stage of the development of the metabolic defect, having already reached the stage of high S_f 6 or even elevated S_f 8 levels. They may, in a shorter period than a corresponding normal group, start to "spill over" into highly elevated S_f 10-to-20 levels, or even S_f 10-to-30. This, if it proves correct, would indicate the likelihood of excessive atherosclerosis becoming a part of the entire life history of the disorder associated with xanthelasma, even though at any one stage excessive atherosclerosis might not be developing, even though the total serum cholesterol concentration is high.

It is interesting to note that patients with xanthoma tuberosum uniformly show exceedingly high levels of the S_f 10-to-20 lipoproteins and S_f 20-to-40 class, in addition to their high total serum cholesterol concentration. This is consistent with their known predisposition to intensive atherosclerosis. In biliary cirrhosis with xanthomatosis, although the cholesterol levels are high, the patient rarely shows any elevation in molecules above the S_f 13 class, the major portion of the serum cholesterol being in the S_f 6, 8, and 10 classes. Probably no group of patients followed carefully with respect to lipoprotein levels and total cholesterol concentrations would be more helpful in the ultimate solution of this problem than patients with xanthelasma.

A rigid animal fat and cholesterol-free diet has effected a decrease of the serum cholesterol level to normal in certain patients,[30] although this has not been found consistently.[31] Such decreases are similar to those occurring in normal persons on similar diets.[30b] Such a dietary also effects a significant decrease in concentration of S_f 10-to-20 lipoproteins.[32] In the absence of such drastically altered dietary regimens the total serum cholesterol level, as well as the level of S_f 10-to-20 molecules, have not been found to be related to the dietary intake of fat and cholesterol over a wide range, either in normal persons,[33] or in those with familial hypercholesteremia,[34] or as attested by this study. Such diets have also been reported

30. (*a*) Footnotes 6*c* and *d*, and 21*b*. (*b*) Keys, A.; Michelson, O.; Miller, E. V., and Chapman, C. B.: The Relation in Man Between Cholesterol Levels in the Diet and in the Blood, Science **112**:79, 1950.

31. Sperry.[8b] Sperry and Schick.[16c] Montgomery.[21b]

32. Gofman, J. W.; Jones, H. B.; Lindgren, E. T.; Lyon, T. P.; Elliott, H. A., and Strishower, B.: Blood Lipids and Human Atherosclerosis, Circulation **2**:161, 1950.

33. Gofman and others.[32] Keys and others.[30b]

34. (*a*) Footnotes 16*b* and 30*b*. (*b*) Wilkinson, C. F.: Essential Familial Hypercholesterolemia: Cutaneous, Metabolic and Hereditary Aspects, Bull. New York Acad. Med. **26**:670, 1950.

to effect an involution of the skin lesions.[6d] On the other hand, there is some evidence that a low caloric intake is the important factor altering the total serum cholesterol concentration and the skin lesions in such dietary regimens.[35] The administration of lecithin has aslo been claimed to effect striking decreases of elevated cholesterol levels,[36] but this has not been confirmed in patients with either xanthoma tuberosum [37] or xanthelasma.[15b]

Extensive genetic studies of families with familial xanthomatosis have shown that hypercholesteremia is the basic disturbance in the inheritance of this syndrome as an incomplete dominant trait,[38] apparently uninfluenced by age or sex.[11b] The heterozygous abnormal person inherits hypercholesteremia with or without xanthelasma,[34b] whereas the homozygous abnormal person inherits hypercholesteremia as well as xanthoma of the skin and/or tendons, sometimes associated with cardiovascular disease due to involvement of blood vessels, endocardium, and even the aortic and mitral valves in rare cases.[39] It may be questioned whether all cases of xanthelasma belong to the syndrome of essential hypercholesteremic xanthomatosis. In families afflicted with the latter syndrome, xanthelasma is commonly found either alone or in members with other cutaneous xanthoma. In such instances xanthelasma would appear properly to belong to this syndrome. On the other hand, xanthelasma is frequently found in patients who fail to exhibit other xanthoma or hypercholesteremia and in whose families cutaneous manifestations other than xanthelasma are not observed. Furthermore, patients with xanthelasma have an associated hypercholesteremia of significantly lower incidence and of less degree than patients with xanthoma tuberosum. It has been suggested by various investigators, in this regard, that essential xanthomatosis is a hereditary familial disorder in which xanthoma tuberosum is the severe form found in homozygous abnormal members and almost always associated with hypercholesteremia, and with cardiovascular involvement frequently present. Heterozygous abnormal members of such families may exhibit only hypercholesteremia without cutaneous xanthoma, the mildest form of the disorder. In similar fashion, patients with isolated xanthelasma may be considered as manifesting a milder form of the same disorder as xanthoma tuberosum.[40] In any event, in the present state of knowledge, all such patients should be carefully observed for the presence of hypercholesteremia and for the development of cardiovascular disease. Furthermore, careful investigation of the members of involved families appears warranted.

SUMMARY

Observations have been made in a group of 35 patients with xanthelasma. Hypercholesteremia was found in 47% and advanced coronary artery disease in at least 20% of these patients. The serum lipoproteins have been analyzed, and

35. Keyes and others.[30b] Curtis, A. C.; Wile, U. J., and Eckstein, H. C.: Involution of Cutaneous Xanthomata Caused by Diets Low in Calories, J. Clin. Invest. **7**:249, 1929.

36. Adlersberg, D., and Sobotka, H.: Effect of Prolonged Lecithin Feeding on Hyperchlesterolemia, J. Mt. Sinai Hosp. **9**:955, 1943.

37. Delevett, A. F., and Bruger, M.: Plasma Lipids in Primary and Secondary Hypercholesteremia: Effect of Lipotropic Substances, Arch. Int. Med. **81**:859 (June) 1948.

38. Footnote 1*b* and *c*. Footnote 11*b*. Footnote 16*b*.

39. Thannhauser.[1a] Fliegelman, Wilkinson, and Band.[11b]

40. Footnote 1*a*, *b*, and *c*. Footnote 2*a*. Footnote 11*b*.

their relationship to the total serum cholesterol concentration and to atherosclerosis has been discussed.

Although xanthelasma is a minor skin lesion, it may be of significance in calling attention to the possibility of an altered cholesterol metabolism and associated atherosclerotic cardiovascular disease. Careful search should be made for possible systemic involvement in all persons with xanthelasma.

450 Sutter St. (8).

655 Sutter St.

1047 Clayton St.

ABSTRACT OF DISCUSSION

DR. U. J. WILE, Ann Arbor, Mich.: This paper is a most interesting and suggestive contribution: It not only increases our knowledge of the origin and significance of xanthelasma, but also it throws a new light on the biochemistry and the bearing of certain blood lipids on the causation of degenerative disease.

To begin with, it appears that what we formerly regarded as a cosmetic defect must, in the light of recent research in blood chemistry, be regarded as a more than occasional forerunner of conditions threatening longevity and life.

It is fitting on this occasion to remind our members of the very significant work done by our late distinguished colleague, Pollitzer, who in 1909, before much was known of the chemistry of blood lipids, determined by microchemistry that the yellow color of xanthelasma was due to infiltration by a fatty substance. His contention that the fat was a degenerative process of muscle was a most natural conclusion in the absence of our knowledge of the nature of the circulating blood lipids.

The recent work of Dr. Gofman, co-author of this paper on the lipoproteins, particularly of the S_f 10-to20 species, is most significant in connection with degenerative circulatory diseases and their relation to blood lipids.

The entire picture of xanthelasma and its evident relation in a considerable percentage of patients to arteriosclerosis, hypertension, and heart disease contains certain curious paradoxes. Hypertension and arteriosclerosis occasionally occur with normal cholesterol blood levels; on the other hand, both are frequently associated with high lipoprotein values of S_f 10-to-20 species. Arteriosclerotic lesions are ordinarily associated with high cholesterol deposits in the lesions themselves, but not necessarily associated with high cholesterol blood levels. High cholesterol blood levels may exist, apparently, without affecting discernible changes in the circulatory system, and thus seem, occasionally, consistent with the maintenance of good health.

The large percentage of patients presented in this contribution in whom the cholesterol levels were well over the normal, and in all of whom the levels were either equal or above the high limits of normal, make it obvious that this previously regarded cosmetic defect may be a forerunner to metabolic changes significantly able to affect the course of normal life.

From one of Dr. Gofman's previous contributions it would appear that it is a proteolipid, which he has dignified by the S_f 10-to-20 species formula, which contributes to degenerative circulatory disease.

In the authors' paper it is not stated that the S_f 10-to-20 species formula contributes to the production of xanthelasma, and it remains to be seen from further research whether this fraction of cholesterol and protein so operates.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I want to congratulate Dr. Epstein and his collaborators on an excellent piece of work. I cannot discuss the Gofman determinations, as there are only three or four places in the country which are equipped to do these studies. I think Dr. Wile was most modest in referring to Dr. Pollitzer because he was a co-author with Pollitzer in one of the original papers on xanthelasma. This term, which was first introduced by these two men, has always been used in this country to refer to xanthoma of the eyelid alone, whereas Siemens and others in Europe use the term, xanthelasma, in a different sense to include all cutaneous xanthomas.

In regard to arteriosclerosis and xanthoma, I have been following a group of patients for some 17 years, and I believe there is definitely a younger age group who, in the early forties or fifties, have increased blood lipids, xanthomas, and cardiovascular disease, whereas the ordinary coronary disease usually develops in the fifties and sixties, and the patients may have perfectly normal blood lipids. Furthermore, in the earlier age group, there is a definite familial history, which was emphasized especially by Müller and more recently by Dr. Fliegelman, Dr. Wilkinson, and Dr. Hand (ARCH. DERMAT. & SYPH. **58**:409-429 [Oct.] 1948), which work was done under Dr. Wile's and Dr. Curtis' supervision.

I shall mention briefly unpublished studies made with one of my former Fellows, Dr. Bart Spence, of Spokane, Wash., of 182 patients seen at the Mayo Clinic who had xanthelasma (xanthoma of the eyelids alone). About 60% of the patients were healthy and had normal blood lipids, 40% had elevated blood lipids, and 25% of the total 182 patients had both elevated blood lipids and cardiovascular disease. In previous studies on xanthoma that I have published, I have stated that 50% of the patients with xanthelasma alone have some elevation of blood lipids, especially cholesterol, and that 50% of those with elevated lipids, or 25% of the total, have evidence of cardiovascular disease. This, therefore, has held true in this larger as yet unpublished series of 182 cases. I was glad also to find that Dr. Epstein in his series had 25% who had cardiovascular disease. In an attempt to follow up the patients in the series with Dr. Spence, we heard from 40% of the patients who were healthy and 40% of those with cardiovascular disease. In the healthy group, of 51 patients heard from, cardiovascular disease subsequently developed in only 4, or 8%, whereas in the group having hyperlipemia and cardiovascular disease, 58% reported that they were much worse, and 3 of the 19 patients had died of heart disease. In my experience, xanthelasma, if seen very early, may involute following a very rigid low animal-fat diet which requires supplement of vitamins. The low animal-fat diet has also been of value in bringing down the blood lipids in both xanthelasma and xanthoma tuberosum and, I believe, has prolonged life in patients having cardiovascular disease in association with xanthomatosis. These findings, I realize, are contrary to recent publications by Ancel Keys, but he was dealing with a group of essentially normal persons.

DR. ERWIN P. ZEISLER, Chicago: I believe this is one of the important papers to be presented before this association. It illustrates again an idea I have had for many years, that if a dermatologist had associated with him not a junior dermatologist but an internist, and if he had a chemical laboratory available, he would be giving his patients better service. The "fly in the ointment" is that a patient who comes to have a simple cosmetic defect removed is likely to resent it if you suggest a complete cardiovascular examination which may prove expensive.

As I look back upon the many patients with eyelid xanthoma that have come to my attention in the past, it seems to me that these patients conformed to a certain physical pattern. Many of them were short, squat, inclined to portliness, and mentally, I should say, below normal. A majority of them were overeaters and men and women well along in years.

The removal of these lesions, especially when extensive, is not an easy procedure, and we cannot always promise permanent results. Dr. Driver just told me they still use trichloroacetic acid as an office treatment and occasionally refer their patients for plastic surgery. Some of the older men present may recall that Dr. Heidingsfeld of Cincinnati, around 1915, came out with the first paper on trichloroacetic acid, recommending it for a variety of benign lesions. My father took to this suggestion and always kept at his right hand a bottle of the deliquescent crystals. The textbooks say to paint it on and then neutralize with alcohol. If I may be permitted a therapeutic suggestion, immediately following the application of the acid it should be etched in with the blunt end of a toothpick before neutralizing it with alcohol. In thicker lesions even a second application may be advisable. Following this a calamine lotion is applied in order to hide the dead-white appearance. The results of this modified technique are usually good, although recurrences may be expected after some months. The solution of this phase of the problem depends upon finding some chemical agent which, when taken internally, will lower the blood cholesterol values to the point at which this chemical change in the tissue about the eyelids no longer occurs.

DR. A. C. CURTIS, Ann Arbor, Mich.: For many years arteriosclerosis has been considered a physiological process brought on by the stress and strain of our life or by a degeneration of our vessels from hypertension. It is becoming more and more apparent that arteriosclerosis is

a disease entity, and I think Dr. Epstein has brought to our attention one of the factors which may play a part in its etiology. He has also shown a possible explanation for a discrepancy and ambiguity which several of us have noted in our studies of patients with xanthelasma (Curtis, A. C., and Berger, J. P.: ARCH. DERMAT. & SYPH. **52**:252 [Oct.] 1945), namely, the normal cholesterol values in 15 to 40% of those who have this disease.

Determination of the total cholesterol or its esters may not be the chemical answer to xanthelasma or arteriosclerosis. S_f 10-to-20 cholesterol, which is not evaluated by such chemical methods, could well be as specific in these diseases as hyperglycemia is in diabetes mellitus.

Xanthelasma should be looked upon as the herald plaque of arteriosclerosis, and those of our patients who have such lesions should be so warned and instructed about diets low in animal fats.

DR. HERMAN SHARLIT, New York: The lipid substances in blood are carried in the circulation both in true solution and as a colloid suspension. The general problem of the deposition of lipid materials in tissues, including the walls of blood vessels, has evoked, among others, studies of the colloidal character of the blood lipids, particularly the stability of these substances as colloidal suspensions. It has long been realized that the measure of the concentration in blood of any one lipid fraction is quite meaningless unless interpreted in the light of the concentration of other fractions. Thus, cholesterol, most difficult to suspend in blood, has a limiting ceiling of concentration in blood determined by the accompanying concentration of the "emulsifying" lipids present, particularly the phospholipid, lecithin.

A few years ago I evolved a laboratory technique calculated to mirror the stability of the lipid suspension in blood samples (*J. Invest. Dermat.* **5**:389, 1942). Currently, using this technique on alcoholic mixtures of purified lecithin and cholesterol, we are demonstrating that for a successful colloidal dispersion of the mixtures in physiologic saline the ratio of cholesterol to lecithin (by weight) approaches 1 as an absolute limit. These findings are in perfect agreement with the statistical deductions from the analysis of lipid fraction estimation in blood samples.

It would seem to me that if the physical status of the blood lipids is a significant factor in the production of lipid deposition in tissues, the arterial tree would be most vulnerable to these influences. By the same reasoning, where a lack of significant positive correlation between cutaneous lipidosis and arterial damage is revealed, we must seek other factors for an explanation of the production of the skin pathology. On the other hand, it may very well be, because of the difficulty of clinically exposing early atherosclerotic changes, that such a pathologic process of the skin as xanthoma may serve to suggest the existence of arterial damage.

The studies here reported by Dr. Epstein have an importance well beyond the skin organ and its pathology.

DR. NORMAN N. EPSTEIN, San Francisco: Dr. Wile, Dr. Montgomery, and Dr. Curtis have emphasized the importance of xanthelasma as an indicator of constitutional disease, especially of the cardiovascular system. It appears evident that a majority of persons with xanthelasma do have a defect in cholesterol metabolism which is familial in origin. The exact nature of this defect is not clear. While hypercholesteremia is common, it is probable that the disturbance in cholesterol metabolism in this group is not necessarily quantitative but may be qualitative and linked with the type of giant lipoprotein molecules of the blood serum transporting the blood lipids. Further studies are necessary to determine the role of the S_f 10-to-20 class of lipoprotein molecules in xanthelasma.

Dr. Sharlit's work on the relation of the various lipids in the blood to each other in maintaining a colloidal suspension is very interesting. It is quite possible that the mechanism which leads to arteriosclerosis may be different from that which is involved in the production of xanthelasma. However, these two phenomena may be intimately related.

I am very glad that emphasis has been placed by the discussants on the part played by Dr. Gofman in this work. I think it is fitting to say that Dr. Gofman has already done outstanding work in this field of medical research.

KOEBNER PHENOMENON IN LICHEN NITIDUS

Report of Two Cases

HERMANN PINKUS, M.D.
MONROE, MICH.
AND
HILLIARD M. SHAIR, M.D.
QUINCY, ILL.

THE CONCEPT of lichen nitidus has gone through several phases of evolution. The first cases were reported by F. Pinkus (1907),[1] who described the condition as a harmless localized and asymptomatic eruption on the shaft of the penis. The granulomatous character of the infiltrate in lichen nitidus stimulated discussion about possible relationship to tuberculosis, particularly after cases had been described in which there was more or less generalized involvement of the skin. Other cases were presented which suggested that lichen nitidus may be a variety of lichen planus (Civatte,[2] Ellis and Hill[3]).

In classic cases, three characteristics of lichen nitidus are outstanding in differentiating it clinically from lichen planus. The first of these is the subjective lack of pruritus as contrasted with the severe itching of most lesions of lichen planus. The second difference is the fact that the eruption of lichen nitidus consists of individual papules which do not become confluent even where they are closely aggregated, while lichen planus papules have a great tendency to coalesce. The third difference is the fact that heretofore the Koebner phenomenon, so characteristic of lichen planus, has received little attention in lichen nitidus. Arrangement of lichen nitidus papules in scratch marks has to our knowledge not been emphasized in the literature and is not mentioned in several textbooks which we consulted. Ormsby and Montgomery[4] write, "No particular arrangement of the lesions occurs."

It is a peculiar coincidence that recently several cases of lichen nitidus with Koebner phenomenon were presented almost simultaneously by independent observers. Grekin[5] presented a case of this kind to the Detroit Dermatological

From the Department of Dermatology, Wayne University College of Medicine (Dr. Pinkus), and the Physicians and Surgeons Clinic (Dr. Shair).

1. Pinkus, F.: Über eine neue knötchenförmige Hauteruption: Lichen nitidus, Arch. Dermat. u. Syph. **85**:11, 1907.

2. (*a*) Civatte, M. A.: Lichen nitidus coexistant avec un lichen planus, Bull. Soc. franç. dermat. et syph. **22**:65, 1911; (*b*) "Lichen nitidus" et lichen planus, Bull. Soc. franç. dermat. et syph. **34**:666, 1927.

3. Ellis, F. A., and Hill, W. F.: Is Lichen Nitidus a Variety of Lichen Planus? Arch. Dermat. & Syph. **38**:569 (Oct.) 1938.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, p. 938.

5. Grekin, J. N.: Lichen Nitidus (with Koebner's Phenomenon), Arch. Dermat. & Syph. **61**:705 (April) 1950.

Society in October, 1948. Pinkus mentioned a similar case in discussion and presented it at one of the following meetings. Omens and associates [6] and Webster and associates [7] each presented a case to the Chicago Dermatological Society in November, 1948, and Wallace [8] presented a case in London at almost the same time. A sixth case was presented in Chicago the following year.[9] Still another case was seen by Shair, and this case and the one presented by Pinkus form the basis of this communication.

REPORT OF CASES

Case 1.—E. H., a 4-year-old Negro girl, was seen on Sept. 20, 1948, with a gradually spreading eruption which was asymptomatic. She complained of pain in the back and abdomen, and the mother thought she had lost weight. Examination showed a well-developed, dark-skinned girl who had scattered groups of round, mostly umbilicated dome-shaped papules of a slightly lighter color than the surrounding skin. Such groups were present on the chest, the back, and the upper

Fig. 1 (Case 1).—Left elbow, showing two lines of lichen nitidus papules which suggest the Koebner phenomenon. The papules are partially confluent; scattered lesions are also present.

and lower extremities. Numerous scattered individual papules were also present. On the forearms, particularly near the elbows, there were several linear groups of papules, apparently arranged in scratch marks (Fig. 1). On the flexor surface of the right leg there were numerous papules forming a broad band which extended from the gluteal fold downward through the middle of the popliteal fossa to the calf. The streak gradually subsided there, tending a little to the mesial side of the leg.

Because of the grouping and the associated systemic symptoms, a presumptive diagnosis of lichen scrofulosorum was made, although lichen nitidus and lichen striatus were considered

6. Omens, D. V.; Omens, H., and Musgrave, D.: Lichen Nitidus, Arch. Dermat. & Syph. **61**:697 (April) 1950.

7. Webster, J. R.; Hetreed, F., and Falk, A. B.: Lichen Nitidus, Arch. Dermat. & Syph. **61**:697 (April) 1950.

8. Wallace, H. J.: Lichen nitidus, Proc. Roy. Soc. Med. **42**:5, 1949.

9. Ebert, M.; Leaf, V., and Musgrave, D.: Lichen Nitidus with Koebner's Phenomenon, A. M. A. Arch. Dermat. & Syph. **63**:805 (June) 1951.

in differential diagnosis. Biopsy of a typical papule from the left forearm showed lichen nitidus. Reaction to a Vollmer patch test with old tuberculin was negative. The systemic symptoms disappeared when the use of cathartics and overindulgence in candy were discontinued, and a multivitamin preparation was administered.

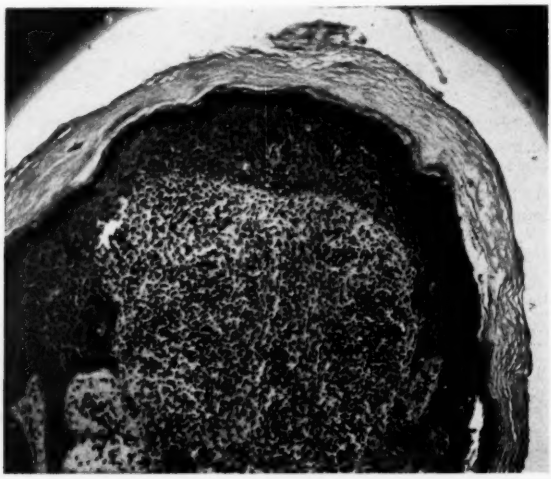

Fig. 2 (Case 1).—Section through the linear lesion caused by the scratch of a pin, showing typical granulomatous infiltrate of lichen nitidus and loss of basal layer of the epidermis. The horny layer is thick because the lesion was situated on the wrist.

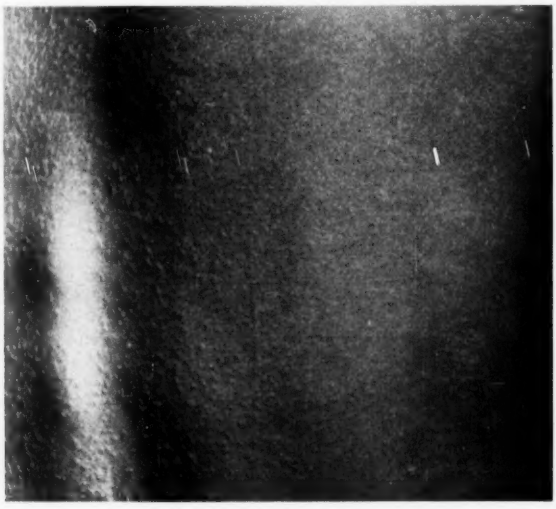

Fig. 3 (Case 2).—Right side of back, showing disseminated lichen nitidus papules and one long line of partially confluent lesions.

Some of the skin lesions were treated with an alcoholic solution containing 75 μc of thorium X per milliliter. These applications were repeated every two weeks and caused considerable hyperpigmentation of the treated areas and gradual fading and flattening of the papules. When

treatment with thorium X was discontinued, the skin gradually returned to its normal hue, and papular lesions reappeared. It could not be ascertained whether these were the former lesions recurring or new ones. During several months of observation some papules tended to disappear spontaneously while new lesions appeared. In December, 1948, the patient's right wrist was accidentally scratched with a safety pin. There was no infection, but when the traumatic crust disappeared, the scratch mark gradually transformed into an elevated streak which was continuous except for one isolated lichen nitidus papule at one end. The streak had the approximate width of lichen nitidus papules, but showed only occasional crosshatching by some deeper skin furrows. Along the top of it there was a fine continuous depressed line. A biopsy specimen was taken from near the center of the streak on Jan. 26, 1949, about six weeks after the scratch had occurred. Microscopic examination showed the typical changes of lichen nitidus (Fig. 2).

CASE 2.—R. DeL., a 13-year-old white boy, was seen on Aug. 28, 1950. During the previous basketball season a slightly itching eruption had developed on the upper and lower extremities. He had previously been treated with potassium arsenite and local remedies, but new lesions continued to develop without any regression of the older lesions. Upon examination, a quite uniform eruption of tiny skin-colored papules was seen to be present from the shoulders to the feet. Where the skin had been scratched, there were long lines of closely set papules, and some

Fig. 4 (Case 2).—Section through a linear lesion from the abdomen, showing the typical features of lichen nitidus.

streaks were continuous (Fig. 3). Two dermatologic lesions, apparently not related to the generalized eruption, were noted. In the left axilla there was a small erythematous elliptic plaque; on the palms and soles there were hyperkeratotic patches. Neither of these lesions caused symptoms, nor had they been noticed by the patient. The complete blood count and results of urinalysis were normal. Reaction to a blood Kahn test was negative. At the patient's next visit 10 days later, the erythematous plaque in the axilla had disappeared. A biopsy specimen taken from a linear lesion on the abdomen showed the typical histologic changes of lichen nitidus (Fig. 4).

COMMENT

The notion that lichen nitidus is a tuberculid has been almost completely abandoned, although Stokes [10] lists the affection as a form of tuberculosis often seen in Negroes. More and more voices favor a relation of lichen nitidus to lichen planus. As Civatte [2b] puts it, there is a syndrome the habitual form of which is lichen planus, while lichen nitidus represents a much rarer variety. Others, like Julius-

10. Stokes, J. H.: Fundamentals of Medical Dermatology, rev. 7, Philadelphia, Department of Dermatology Book Fund, University of Pennsylvania School of Medicine, 1942, p. 403.

berg,[11] stress the differences between the two conditions, particularly the fact that while the early stages of a lichen planus papule may resemble lichen nitidus clinically as well as histologically, the planus papule will develop into other stages while the nitidus papule is monomorphous and does not change. Sachs [12] just recently said in discussion that he cannot agree that lichen planus and lichen nitidus are in any way related. It is not the place here to enter this controversy. The main purpose of this presentation is to call attention to the occurrence of the Koebner phenomenon or isomorphic effect of irritation in lichen nitidus, and to the peculiar coincidence that this phenomenon was observed independently by several clinicians in a half dozen cases within the last two years. In one of our cases, the development of lichen nitidus from an accidental pin scratch could be followed and confirmed by biopsy. Why this occurrence has not been announced before is hard to say. It is difficult to believe that it would not have been described by any of the careful early authors if they had seen it. The only reference which might be construed as referring to linear lesions, and which was so interpreted by Falk,[13] was made by Civatte,[2a] but apparently these lesions were an incidental finding (subsiding purpura?) in his case. In Ellis and Hill's second case of combined lichen planus and lichen nitidus [3] the Koebner phenomenon was present, but biopsy of one of the linear lesions revealed lichen planus, and the authors based the diagnosis of lichen planus in part on the occurrence of linear lesions. From the recent series of cases of typical lichen nitidus exhibiting the isomorphic response to stimulation, we must now conclude that the Koebner phenomenon cannot be used for differential diagnosis of the two lichens.

In addition to linear arrangement of individual papules, our patients exhibited some other unusual features. There was a broad streak of papules down the flexor surface of one lower extremity in Case 1, similar to the configuration of lichen striatus. The same patient exhibited definite grouping of lesions on the trunk, as it is commonly seen in lichen scrofulosorum. In both patients, some of the Koebner-type lesions consisted not of individual papules but of confluent ones.

Arrangement of lichen nitidus in the shape of a systematized streak has not been described previously to our knowledge, but the flexor surface of thigh and leg is a site with predilection for a variety of "linear" dermatoses.[14] In addition to lichen striatus, cases of lichen planus, lichen simplex chronicus, and even lichen scrofulosorum with this arrangement, which corresponds to Voigt's inner boundary line of segmental nervous distribution, have been described. Grouping has been described in lichen nitidus. Barber [15] called attention to pityriasiform and psoriasiform patches in his patients, thus indicating not only grouping but confluence as well. The patches in our Case 1 consisted definitely of individual papules. Confluence was observed only in the linear lesions, and particularly in the one that followed a rather deep scratch with a safety pin. In this case there was not coalescence of primary elements,

11. Juliusberg, F.: Lichen ruber und Pityriasis rubra pilaris, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, Vol. 7 (Pt. 2), p. 125.

12. Sachs, W., in discussion on Sharlit, H.: Lichen Nitidus and Lichen Planus in a Man Aged 19 Years, Arch. Dermat. & Syph. **63**:518 (April) 1951.

13. Falk, A. B., in discussion on Webster, Hetreed, and Falk.[7]

14. Pinkus, H.: Lichen Striatus and Lichen Planus, J. Invest. Dermat. **11**:9, 1948.

15. Barber, H. W.: Lichen nitidus, Bull. Soc. franç. dermat. **34**:664, 1927.

but the entire scratch transformed into lichen nitidus in toto, so to say, into one giant linear papule. F. Pinkus [16] leaned toward the opinion that the primary lesion in lichen nitidus is damage to some basal cells which is followed by a foreign-body type of reaction. If we agree with this opinion, we can easily understand that a deep scratch which damages the basal layer may lead to such a confluent reaction.

SUMMARY

Two cases are presented of lichen nitidus exhibiting the Koebner phenomenon of isomorphic response to trauma. Attention is called to the fact that five other cases were recently presented by other observers, and that the Koebner phenomenon can no longer be considered as a differential characteristic between lichen nitidus and lichen planus.

12 E. Fourth St.

1101 Maine St.

16. Personal communication to the authors.

XANTHOMA DISSEMINATUM

An Unusual Form with Extension of Xanthomatous Changes into Muscle

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WHITE PLAINS, N. Y.
AND
ABRAHAM I. WEIDMAN, M.D.
BROOKLYN

XANTHOMA disseminatum is an entity that is infrequently encountered. It represents a systemic disorder involving the reticuloendothelial system, particularly the reticulum cells and the histiocytes. It differs in the main from xanthoma tuberosum in that the blood serum cholesterol is normal or low [1] and the lesions are more commonly found on the flexural surfaces of the skin.

In addition to skin involvement, many other organs and tissues have been found with xanthomatous changes. Lesions have been demonstrated on the mucosal surface of the mouth, epiglottis, and larynx, on the cornea and sclera,[2] in the pleura, lungs, pituitary gland, and the tuber cinereum,[3] in bones, spinal cord, lymph glands, and spleen,[4] in the brain,[5] in the liver,[6] and on the serous surfaces of the pericardium and peritoneum, the walls of the esophagus, stomach, and intestinal mucosa, as well as in glands (thymus, pancreas, and adrenals).[6a] Thannhauser [6c] has indicated that xanthomatous nodules may originate in every organ where reticulum cells and histiocytes are normally present.

The case herein reported is an unusual instance of primary essential xanthomatosis of the normocholesteremic type with marked extension of xanthomatous

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From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman), and the Skin and Cancer Unit of the University Hospital.

1. Thannhauser, S. J., and Magendantz, H.: The Different Clinical Groups of Xanthomatous Diseases: A Clinical Physiological Study of *22* Cases, Ann. Int. Med. **11**:1662, 1938.

2. Pusey, W. A., and Johnstone, O. P.: A Case of Xanthoma Diabeticorum and Lipoma Multiplex, and a Case of Xanthoma Approaching the Diabetic Type with Diabetes Insipidus, J. Cutan. Dis. **26**:552, 1908.

3. Turner, A. L.; Davidson, J., and White, A. C.: Xanthomatosis: Some Aspects of Its Blood Chemistry and Pathology, Edinburgh M. J. **32**:153, 1925.

4. Horsfall, F. L., Jr., and Smith, W. R.: Schüller-Christian Syndrome: Lipoid Granulomatosis: Defects in the Bones, Exophthalmos and Diabetes Insipidus, Quart. J. Med. **6**:37, 1935.

5. Weidman, F. D., and Freeman, W.: Xanthoma Tuberosum: 2 Necropsies Disclosing Lesions of the Central Nervous System and Other Tissues, Arch. Dermat. & Syph. **9**:149 (Feb.) 1924.

6. Thannhauser, S. J.: (*a*) Lipidoses: Diseases of the Cellular Lipid Metabolism, in Christian, H. A.: Oxford Loose Leaf Medicine, New York, Oxford University Press, 1940, Vol. 4, pt. *2*, Chap. 7-A, p. 136; (*6b*) ibid., p. 137; (*6c*) ibid., p. 149.

changes into both skeletal and myocardial muscle tissue as well as other organs. To the best of our knowledge a similar case has not been previously reported.

REPORT OF A CASE

T. P., a 72-yr.-old Jewish woman, was admitted to the University Hospital on Aug. 24, 1949. She stated that about two years before admission she suffered from a "bad cold" and

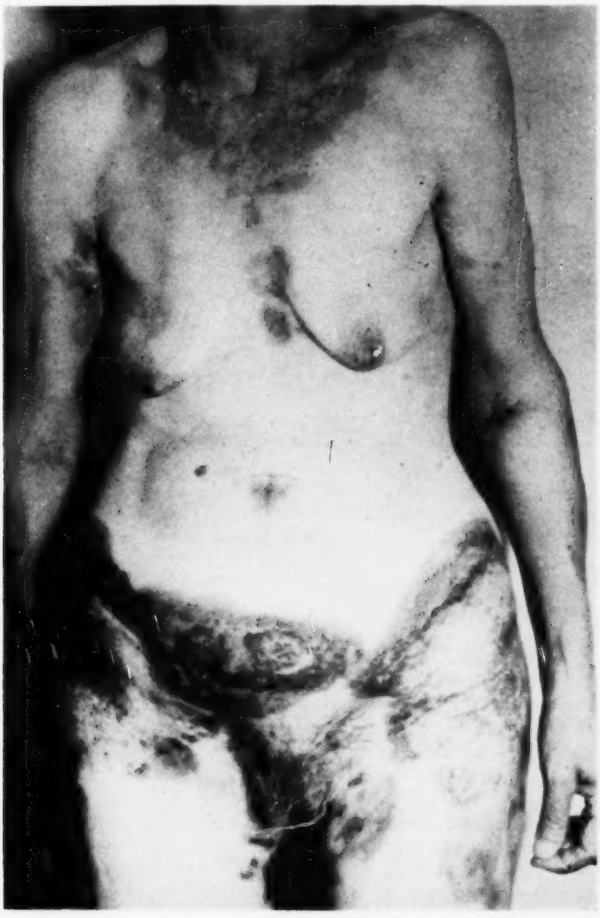

Fig. 1.—Generalized character of the skin lesions.

fever. After recovery she began to lose weight and noticed the appearance of lesions first on the neck and then on the lower abdomen and in the groins. There were no other significant points in the past medical history.

The patient was underweight. Physical examination revealed many small isolated pea-sized yellow nodules on both sides of the neck, both antecubital fossae, and the upper chest. The lower neck and the "V" area of the chest were covered with a pink-yellow infiltrated area studded with yellow papules. On both forearms and arms, extensor surfaces of the thighs, and lower

abdomen there were many firm hard patches. The lesions on the extremities and abdomen were firmly fixed to the underlying structures and were scleroderma-like to palpation. The more recent lesions were on the anterior wall of the abdomen. In some areas on the forearms and the lateral surfaces of the thighs, where the skin was rigid, the lesions adjacent to normal skin had a corrugated appearance (Fig. 1).

There was a systolic murmur audible at the apex. The blood pressure was 180/90. The abdomen was soft. The liver was palpable 5 fingerbreadths below the right costal margin. The spleen and lymph nodes were not palpable.

Laboratory Findings.—A hemogram revealed the following findings: red cells, 3,460,000; hemoglobin, 10.2 gm. per 100 cc.; white cells, 10,750, and a normal differential count. The urine was normal. The icteric index was 6 units. Reactions to van den Bergh tests, direct and indirect, were negative. The result of the cephalin-cholesterol flocculation test was 4+. The thymol turbidity test showed 9 units. The total protein was 5.0 gm. per 100 cc. (albumin 3.2 and globulin 1.8). Creatinine in the urine was 0.663 gm. per 24 hr. (normal, 1.0 to 1.5 gm.), and creatine in the urine was 0.206 gm. per 24 hr. The result of the sulfobromophthalein sodium test was normal. The cholesterol findings were slightly subnormal, revealing a total of 145 mg. per 100 cc. of total cholesterol, of which cholesterol esters were 95 mg. per 100 cc. and free cholesterol 50 mg. per 100 cc.

Two portions of skin, with underlying subcutaneous and muscle tissue, were removed for microscopic examination, one from the left thigh and one from the right forearm. The specimens included skin from areas that had the scleroderma-like firmness. The left thigh lesion included skin that was corrugated as well as scleroderma-like. The findings in both preparations were the same. The histopathological preparations were described by Dr. Arthur B. Hyman as follows:

"The epidermal changes are insignificant. The upper cutis shows basophilic degeneration of the elastica. The infiltrate is composed of histiocytes, scattered foam cells and multinucleated cells, some foamy and other foreign-body-type giant cells, as well as polymorphonuclear leukocytes. The vessels in the midcutis have very thick walls. There are widely scattered areas of necrobiosis, with homogenization of connective tissue, surrounded by an infiltrate with the above-mentioned cells. The deep cutis shows striated muscle fibers which themselves are not affected. However, insinuated between the bundles there are infiltrates again of the above-mentioned cells. Microscopic diagnosis is extensive xanthomatous infiltration of skin, subcutis, and muscle" (Fig. 2 and 3).

A punch biopsy of the liver was performed, and the histopathological examination showed no abnormal changes.

The wound on the right forearm, where tissue had been removed for microscopic examination, healed by primary intention. The thigh wound, however, failed to heal, leaving a persistent ulcer. In Sept., 1949, small ulcers appeared in the xanthomatous skin on the anterior abdomen. With the cooperation of Dr. Eugene Saberski, Tarrytown, N. Y., the ulcers on the anterior abdomen and thigh were held in check with various agents. Zinc oxide paste, cod liver oil ointment, 2% aqueous solution of methylrosaniline chloride (gentian violet), penicillin given parenterally and topically, streptomycin given intramuscularly, aureomycin given orally, sulfathiazole given topically, and superficial x-ray therapy were used. The patient also received oral vitamin-E therapy, nicotinic acid, multivitamin therapy, and priscoline.® Some of the ulcers would heal only to break down and new ones appear. In April, 1950, ulcers appeared on the upper extremity in xanthoma-involved skin, and those on the abdomen and thigh began to extend and become confluent. Pain became severe, not only present in areas where the skin was broken down but also in deep areas where muscle infiltration apparently existed. Codeine sulfate, meperidine (demerol®), hydrochloride, pantopon® (a preparation of the soluble hydrochlorides of opium in their original proportions but with no inert material or resins), and morphine were needed to control pain.

The patient was hospitalized on June 20, 1950, at the White Plains Hospital. At this time the ulcers were present on the entire lower anterior abdomen, on the sides of the thighs, and on the forearms and arms. The laboratory findings were: red cells, 3,900,000; hemoglobin, 9.8 gm.; and white cells, 6,200, with 85% polymorphonuclear leucocytes. The urine had a specific gravity of 1.030, with a heavy trace of albumin and an occasional red blood cell. The plasma protein was 5.1. The hematocrit was 30%.

Zinc peroxide dressings were used and bacitracin was applied to the edges of the ulcer by Dr. Rockwood Keith, Scarsdale, N. Y. With this therapy there was some evidence of epithelization in some of the margins of the ulcers. The patient had a moderately febrile course until the seventh day of hospitalization, when the temperature rose abruptly to 104.6 F. The rise continued through the night, reaching 107 F. terminally on the following morning.

Postmortem examination performed by Dr. Homer Kesten at the White Plains Hospital revealed the following findings: (1) generalized xanthomatosis with ulcerations; (2) acute bronchitis; (3) early lobular pneumonia; (4) lipid depletion of adrenals; (5) generalized arteriosclerosis; (6) sclerosis of pulmonary arteries; (7) serous cystadenoma of left ovary; (8) polyp of the endometrium; (9) obsolete apical tuberculosis of lungs; (10) tuberculosis of the mesenteric lymph nodes, and (11) leiomyoma of right kidney.

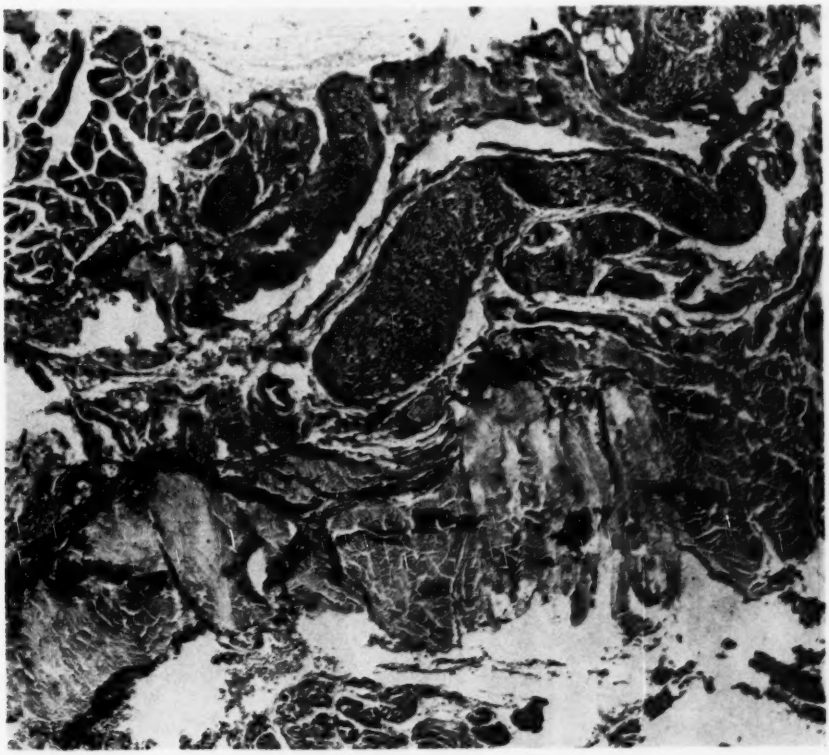

Fig. 2.—Xanthomatous infiltrate at level of and between bundles of striated muscle.

Dr. Kesten reported the following findings in the microscopic examinations: "The section of the skin ulcer on the left thigh showed areas partly covered by a largely regenerated keratinizing stratified squamous epithelium that shades off along one edge into pre-existing epithelium. The new epithelium lacks rete pegs and at the edges of the ulcer becomes quite thin and somewhat edematous along the basal layer. It also bears masses of polymorphonuclear leucocytes and shreds of partly detached keratin. Where the epithelium is missing, the surface consists of granulation tissue that appears relatively old, to judge from the amount of collagen between the vessels. On the surface of this denuded portion of the section are masses of polymorphonuclear leucocytes and amorphous granular basophilic material, probably zinc peroxide. Beneath this superficial ulcer base is a quantity of fibrous and fatty tissue infiltrated by large numbers of

inflammatory cells of all types. These include lymphocytes, a few plasma cells, and innumerable histiocytes. Many of the latter are swollen and have a pale, finely foamy, lipid-containing cytoplasm. Cells with similar cytoplasm are also found to contain more than one nucleus, and in the deeper portions of the specimen there are great numbers of such multinucleated cells, some of

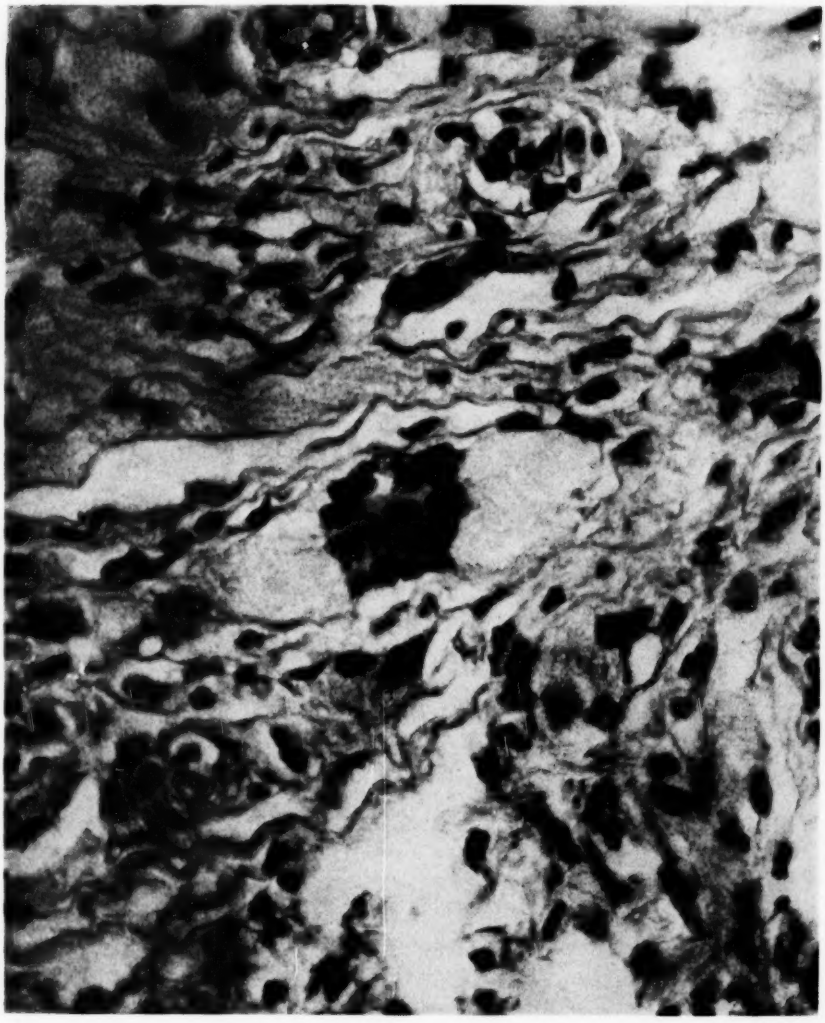

Fig. 3.—Xanthoma foam cells and xanthomatous giant cells of the infiltrate, showing minute details of their structure.

which have a foamy cytoplasm and some a more compact eosinophilic cytoplasm. These are accompanied with histiocytes and lymphocytes, many of the former swollen and fat-containing. This is especially striking in the lobules of fat tissue that are attached and surrounded by bands of collagen. The infiltration extends to the deepest portion of the specimen which represents the deepest layer of the subcutaneous tissues. The vessels present are enclosed in fibrous and

fatty tissue, and this too is infiltrated by fat-laden histiocytes and by multinucleated cells of the Touton type, as described above. Underneath the intact epithelium at the margin of the ulceration, the corium is similarly infiltrated by wandering cells of all types, including great numbers of Touton cells. At this level there are also irregular zones in which the collagen appears to be swollen, fragmented, and necrotic, and each remaining collagen fiber is surrounded by nuclear dust and granular eosinophilic material. This zone of necrosis is sharply limited to the corium and the first portion of the subcutaneous tissues. Beneath it the deeper tissues are infiltrated in a manner similar to that previously described beneath the ulceration proper.

"Specimens taken through the muscle beneath the ulcerating lesions on the left thigh and the anterior abdomen show considerable atrophy of muscle bundles with fragmentation of many of the remaining fibers. The sarcoplasm in the remaining fibers tends to be swollen and eosinophilic, and it exhibits numerous small fissures and cracks. The cross striations are indistinct. The accompanying connective tissue contains a few lymphocytes, occasional foamy phagocytes, and multinucleated cells of the Touton type.

"A section of supposedly normal muscle from the wall of the thorax reveals foci of xanthomatous infiltration in the connective tissue between relatively normal muscle bundles.

"Lymph nodes from the left inguinal region, although normal in size, reveal an indistinct architecture. The nodes are enclosed in a large amount of fibrous and fatty tissue that is infiltrated by foamy cells. The lymph nodes themselves contain only lymphocytes with a few plasma cells around the periphery. There is no increase in reticulum cells, and no foam cells are found within the nodes proper, but the fibrous bands that enter the nodes and carry vessels are infiltrated by lymphocytes and plasma cells.

"Examination of the left ventricle of the heart shows the myocardium normal for the most part, but adjacent to several of the small myocardial arteries are small infiltrations of lymphocytes and histiocytes, and at one point there is a diffuse interstitial fibrosis with infiltration of the fibrous tissue by lymphocytes, histiocytes, some of which are foamy, and occasional multinucleated cells. A similar infiltration is found in the attached epicardium.

"In the lung the alveolar capillaries are congested. A few alveoli contain polymorphonuclear exudate, and similar exudate together with erythrocytes is found in accompanying small bronchi. The larger vessels in this block present no unusual changes. In the gross, the lung reveals apical tuberculosis scar formation.

"The venous sinusoids of the spleen are widely distended, but they appear to be empty for the most part. The intervening pulp cords are poor in nuclei. The malpighian bodies are normal. In the sinusoids are lymphocytes and quite numerous histiocytes, some of which have coarsely vacuolated cytoplasm.

"The liver cells are intact. Glycogen nuclei are abundant. The sinusoids are slightly wider than normal and contain a moderate amount of blood, together with unusually numerous lymphocytes. No foam cells or multinucleated elements are present either in the sinusoids or in the entirely normal portal areas. The Kupffer cells are normal.

"The small veins of the pancreas are greatly congested. The interstitial tissue is focally hemorrhagic, but there are no infiltrations beyond a few lymphocytes. The parenchyma is intact.

"The cortical cells of the adrenal glands are virtually devoid of lipid. The sinusoids are congested. The medulla is normal. There is a little sclerosis of the periadrenal arterioles, and the accompanying fat is edematous but free of infiltration.

"A nodule noted grossly in the right kidney proved to be an unencapsulated but well-circumscribed mass of smooth muscle tissue arranged in anastomosing delicate bundles, with a small amount of stroma. There are only a few blood vessels in it. The renal parenchyma except for congestion is normal, and the accompanying pelvis is normal.

"The polyp of the uterus is made up of a quantity of fibrous stroma containing a few smooth muscle bundles and enclosing innumerable cystic glands filled with mucus and lined by a single layer of cuboidal cells. The surface epithelium is also flattened.

"The left ovary contained a cyst lined by a single layer of flattened epithelial cells supported by a fibrous stroma, attached to which is a small amount of fat and fibrous tissue. The latter elements are infiltrated by foamy phagocytes and by multinucleated cells similar to those described in the xanthomatous lesions elsewhere.

"The marrow of the lumbar vertebra is quite cellular and contains all of the usual elements in normal proportions. There is no increase in multinucleated elements, those present being megakaryocytes, and no foamy cells are seen.

"The parenchyma of the thyroid appears essentially normal. There are a few small infiltrations of lymphocytes but no xanthomatous infiltration. The attached fibrous and fatty tissue, however, is infiltrated in a manner similar to that previously described. A small branch of the thyroid artery exhibits calcification along and just outside the internal elastic lamella. Skeletal muscle attached to the thyroid artery is also infiltrated at its margin by multinucleated cells having deeply staining nuclei, and these are accompanied by foamy histiocytes."

SUMMARY

A case of xanthoma disseminatum is reported. This report includes both the clinical and the postmortem findings.

Xanthomatous changes were observed in the connective tissue of the skeletal muscle underlying involved and noninvolved skin. These changes were also noted in the interstitial tissue of the myocardium, in the wall of an ovarian cyst, and about the inguinal lymph nodes.

Medical Centre.

255 Eastern Parkway.

Clinical Notes

CORTICOTROPIN (ACTH) ADMINISTERED INTRAVENOUSLY

BEN KANEE, M.D.
VANCOUVER, B. C., CANADA

A recent article by Mandel and his associates [1] reported on the intravenous use of "pituitary adrenocorticotropic hormone (ACTH)," corticotropin. One wishes to confirm the efficacy of this mode of administration in the treatment of dermatologic problems, especially in acute edematous dermatitides, such as contact dermatitis, dermatitis medicamentosa, and erythema multiforme, in which treatment given over four to eight days is generally followed by a marked if not dramatic improvement. Other diseases, such as pemphigus, atopic eczema, and psoriasis, likewise respond to this manner of using corticotropin but tend to relapse on cessation of treatment. Prolonged medication with this drug demands the usual careful observation in regard to the known undesirable reactions that can occur.

An outline of treatment is as follows: Ten milligrams of corticotropin is dissolved in 1,000 cc. of 5% dextrose in water and given as a continuous intravenous drip of 15 to 20 drops per minute over a 20-to-24-hour period, and repeated daily, using 5 mg. of corticotropin. This is supplemented by a salt-free diet and oral administration of potassium chloride, 1 to 2 gm. three times a day, in an attempt to prevent disturbances of electrolyte metabolism. Concomitant local treatment is not generally necessary.

This short-term plan of treatment offers great and immediate comfort to distressed patients and is a very economical method of using corticotropin to help shorten the morbidity of many diverse dermatological conditions.

607 Birks Bldg.

1. Mandel, W.; Singer, M. J.; Gudmundson, R.; Meister, L., and Modern, F. W. S.: Intravenous Use of Pituitary Adrenocorticotropic Hormone (ACTH): A Report of Its Administration in 25 Patients, J. A. M. A. **146**:546-551 (June) 1951.

TRICHOPHYTON SULFUREUM CAUSING ERYTHEMA NODOSUM AND MULTIPLE KERION FORMATION

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ERNST M. ROSENBAUM, M.D.
AND
EDWARD H. MANDEL, M.D.
NEW YORK

A kerion caused by Trichophyton sulfureum was recently reported by Moore and Woolridge.[1] We are reporting a case of multiple kerion formation and erythema nodosum caused by this species of fungus.

REPORT OF A CASE

A 9-year-old boy from Puerto Rico was admitted to the New York Skin and Cancer Hospital on Jan. 19, 1950. He complained of an eruption of the scalp which had been present

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the New York Skin and Cancer Hospital.

1. Moore, M., and Woolridge, W. E.: Kerion Caused by Trichophyton Sulfureum: Report of a Case, Arch. Dermat. & Syph. **61**:460-465 (March) 1950.

for three weeks. The lesions were first noticed after a haircut. The patient's mother was of the opinion that penicillin administered orally aggravated the condition. Examination of the back of the scalp showed multiple pea-to-chestnut-sized abscesses. A palm-sized erythematous boggy pustular plaque extended from the occiput to the nuchal region. Discrete papulopustules, some of which were follicular, were also present on the patient's back. Similar discrete lesions were symmetrically distributed over the malar areas of the face.

The lower extremities presented erythematoviolaceous tender plaques made up of pea-sized nodules. These lesions had the appearance of erythema nodosum. These plaques extended over the pretibial aspects from below the knee to the proximal portion of the ankle and laterally to the midline. Mycologic data were as follows: Filtered ultraviolet rays did not reveal any abnormal fluorescence. Repeated examinations of hairs in potassium hydroxide preparations failed to show hyphae. Some of the scales obtained from the scalp were planted on Sabouraud's dextrose agar. A growth appeared within a week. At first a primrose substrate with small raised granular convoluted colonies was noted. These colonies were cream-brown, and after they had coalesced, a convoluted chain of colonies was produced. The sulfur-yellow color did not appear in the primary culture. A transplant started to grow within a few days, producing a central raised convoluted area with a light-yellow color present on the mycelium. Surrounding this yellow convoluted area was a fine white powdery mycelium. Deep radial grooves extended from the center of the culture almost to the periphery. The substrate pigment was dark-brown. The culture mount revealed mycelial elements, chlamydospores, and occasional microconidia.

An intracutaneous injection of 0.05 cc. of 1:30 trichophytin (Lederle Laboratories) elicited an immediate wheal reaction after 15 minutes, and after 48 hours, a papular tuberculin-type positive reaction.

The lesions on the scalp healed after compresses with saturated solution of boric acid had been applied for approximately two weeks. These compresses were applied six times for one-half-hour periods. The erythema-nodosum-like lesions on the leg and the papulopustular eruption on the face and back regressed spontaneously one week after treatment with boric acid compresses was started on the scalp. A small abscess appeared on the scalp on Feb. 15, 1950, four weeks after treatment had been started. The lesion cleared a month later after ammoniated mercury ointment (5%), salicylic acid ointment (3%), and bacitracin ointment had been applied in turn. Tests of hair pulled out of the small abscess on Feb. 15 elicited negative results, microscopically and culturally. Further examinations done monthly up to July, 1950, showed hair and scales negative for fungi at all tests.

COMMENT

Typical findings in the T. sulfureum infections are a patchy alopecia of the scalp, with or without scaling, and circinate lesions of the glabrous skin.

Mycologic findings are essentially as follows: the presence of large-spore endothrix hairs without diagnostic fluorescence under Wood's light; the presence of a primrose color in the substrate with a convoluted culture in a primary growth, then the appearance of a light sulfur-yellow color, and the absence of diagnostic features in the culture mount.

Scalp infections without kerion formation caused by T. sulfureum may be recalcitrant to topical medication, and x-ray epilation may be required. The lesions on the glabrous skin usually respond to topical applications of ammoniated mercury ointment (5%).

The development of multiple kerion formation is rare in T. sulfureum infections. The association of erythema nodosum with this dermatomycosis is even more unusual, and the concurrence of multiple kerion formation and erythema nodosum is most unusual.

Erythema nodosum or nodosum-like lesions may appear either in the presence or absence of kerion formation. The first case with kerion formation was reported by Bruno Bloch.[2] The causative agent in the latter's case was Trichophyton gypseum. We had the opportunity to observe with Dr. M. Jessner a patient with kerion formation due to Candida (Monilia) lanosum associated with a papulofollicular eruption on the chest and erythema-nodosum-like lesions on the lower extremities.

2. Bloch, B.: Die Trichophytide, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, Vol. II, p. 583.

Erysipelas-like reactions may arise in the absence of kerion formations as "ids," secondary to a primary fungous infection of the feet.[3] These lesions are usually on one leg and are located close to the primary infection. The possibility that a mycotic infection may have opened up channels for the invasion by streptococci or other pyogenic organisms should also be entertained. The reaction may be initiated by trauma. The 48-hour-trichophytin reaction may or may not be positive in these cases.

Treatment of the primary focus in previously reported cases has been followed by clearing of the erysipelas-like eruptions of the lower extremities.[4]

SUMMARY

A case of multiple kerion formation and erythema nodosum of the lower extremities due to Trichophyton sulfureum has been reported. The nodose lesions healed spontaneously with involution of the kerion.

60 Gramercy Park W. (10).

5 W. 86th St. (24).

1082 Park Ave. (28).

3. Traub, E. F., and Tolmach, J. A.: An Erysipelas-like Eruption Complicating Dermatophytosis, J. A. M. A. **108**:2187-2189 (June 26) 1937.

4. Sulzberger, M. B.; Rostenberg, A., Jr., and Goetze, D.: Recurrent Erysipelas-like Manifestations of the Legs, J. A. M. A. **108**:2189-2193 (June 26) 1937.

BLACK HAIRY TONGUE

Report of a Case Cured with Superficial Roentgen Radiation

D. TRUETT GANDY, M.D.
HOUSTON, TEXAS

Black, hairy tongue is a disorder of curious morphology, which, although first described more than a century ago, continues to arouse interest because of its oddity and disputed origin. It is probably more common than has been generally supposed. Mild degrees of the condition doubtless pass unrecognized.

This malady may occur anywhere on the dorsum of the tongue, but in a typical example it arises in the triangular area in front of the circumvallate papillae and slopes forward as a dark fusiform mass, composed of elongated epithelial filaments, with a tendency to branching, giving the superficial impression of a tuft of hairs. The appearance has been appropriately likened to "the hair of a dog dampened by water" and "a field of corn laid low by the wind." The individual elements of the lesion, which may reach ¾ in. (1.91 cm.) in length, represent hypertrophic filiform papillae, and the color may range from black through sepia-brown to yellowish and even greenish hues.

The pigmentation has been ascribed by different authors to various micro-organisms, and to external sources, such as foods, stimulants, and mouth washes, and several hypotheses have been postulated in attempts to explain the remarkable overgrowth of the papillae. Histologically, the process is essentially a hyperkeratosis, showing no evidence of inflammatory reaction. The course is capricious. Spontaneous involution may occur followed by recurrence. The filaments are usually tough and difficult to detach by pulling. Certain patients may complain of tickling sensations or slight gagging, but most cases are asymptomatic and therefore of no great clinical significance. Introspective persons may develop fancied symptoms, such as a mawkish taste and even pain, once their attention has been directed to the presence of the condition.

The treatment usually recommended is manual removal of the filaments followed by application of mild cauterants, such as 10% salicylic acid in alcohol [1] and trichloroacetic acid.[2] Because of its specific action on epithelial hypertrophies the use of massive-dose vitamin-A therapy would seem rational, and this has been tried [3]; but the lesion is prone to recur. Success with superficial roentgen-ray therapy in a patient of mine prompts the following report.

REPORT OF A CASE

On May 1, 1949, W. P., a white man, aged 55, came seeking advice about a "growth on the tongue." He was not able to say how long it had been present. He discovered it accidentally when trying to look at his throat in the mirror, and had since been periodically conscious of mild gagging sensations. The history was otherwise noncontributory.

Examination revealed a cluster of bluish-black, hair-like, intertwining strands in front of the "V" formed by the circumvallate papillae, arising close together but free at their opposite ends and tapering forward in the midline of the dorsal tongue surface (Fig.). The mass lay in a slimy deposit. Pushing it about with a tongue depressor made the "hairs" bristle up, and some were easily plucked loose while others resisted traction. Many were ½ in. (1.27 cm.) long.

Typical lesion of black, hairy tongue.

The lesion was treated with 300 r of unfiltered superficial roentgen rays through a cone with 1-in. (2.54 cm.) port, the beam being directed at the base of the triangular mass in the circumvallate V. The growth disappeared in 10 days and has not recurred after two years.

SUMMARY

1. The clinical characteristics, symptoms, course, and treatment of black hairy tongue are discussed briefly.

2. A case is reported in which the condition has not recurred for two years after treatment with unfiltered superficial roentgen rays.

424 Medical Arts Bldg. (2).

1. Prinz, H., and Greenbaum, S. S.: Diseases of the Mouth and Their Treatment, ed. 2, Philadelphia, Lea & Febiger, 1939, p. 479.

2. Wise, F., in discussion on Cipollaro, A. C.: Black Hairy Tongue, Arch. Dermat. & Syph. **48**:432 (Oct.) 1943.

3. Lascaris, T., and Curtis, G. D.: Concerning the "Parasitic" Etiology of Hairy Tongue, J. Invest. Dermat. **13**:99, 1949.

PIGMENTED HAIRY TONGUE ACCOMPANYING ANTIBIOTHERAPY

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SPRINGFIELD, MO.

Woods and associates [1] and others have called attention to "monilial infections complicating the therapeutic use of antibiotics."

During the last several months I have observed something which, as far as I know, has not been observed or at least reported. This is in regard to the probable causation of the pigment in black and brown hairy tongue cases.

A patient with an apparently normal tongue was given penicillin by intramuscular injection. Two days later, because of a "cold," she began taking an iron-containing patent medicine.[2] She then reported that her tongue "turned brown and then black" after the use of this patent medicine was begun. This interested me, and, wondering if iron in the medication caused the pigmentation, I gave myself 300,000 units of penicillin intramuscularly while my own tongue was apparently normal. It became covered with Candida albicans, and I then took some samples of an iron-containing antianemia tablet.[3] Overnight my tongue became covered with brown-to-black pigment in the coating. It would have been clinically indistinguishable from "black hairy tongue." I have observed this in myself and in several patients repeatedly.

It is apparent, in a comparatively few cases, that iron causes pigment to appear in a hairy tongue. It is quite possible that other metals may do likewise. Further study seems desirable.

The observation that antibiotics allow Candida (Monilia) to grow luxuriantly has been repeatedly made.

This note gives an explanation as to why some such cases are brown or black, namely, the presence of iron in large amounts taken in the diet or as medication.

ADDENDUM

This phenomenon has, after the above note was submitted, been observed following the use of aureomycin and terramycin, but no opportunity has been afforded to observe whether or not it follows the use of streptomycin, neomycin, tyrothricin, bacitracin, or chloramphenicol.

631 Cherry St.

1. Woods, J. W.; Manning, I. H., Jr., and Patterson, C. N.: Monilial Infections Complicating the Therapeutic Use of Antibiotics, J. A. M. A. **145**:207-211 (Jan. 27) 1951.

2. This preparation was the widely advertised "hadacol."

3. These tablets were feosol,® Smith, Kline & French Laboratories.

CONTACT DERMATITIS FROM SILICONE PUTTY

RAYMOND C. V. ROBINSON, M.D.
BALTIMORE

Silicon, like carbon, is quadrivalent, and thereby may form an infinite number of chemical substances. A group of such substances, combining carbon, oxygen, and silicon and known as silicones, possesses peculiar physical properties which lend themselves to uses in medicine and industry.

A recent issue of *The Journal of the American Medical Association* [1] describes one of the silicones as acceptable for use in "some kinds of therapeutic exercise for the hands." This particular substance has a putty-like consistency which is not affected by temperature changes (from 0 to 100 degrees C.). Given time, it will assume the shape of its container. If dropped it will bounce, but, if struck a sharp blow, it may shatter.

1. Silicone Bouncing Putty Accepted, report of the Council on Physical Medicine and Rehabilitation, J. A. M. A. **146**:817 (June 30) 1951.

One property not described by the *Journal* is the ability to pick up such things as print from a newspaper or comic book. The case of a recent patient affected by the latter property seems worthy of presentation, since at least one manufacturer has made available a small plastic container of this bouncing, putty-like material as a toy.

B. D., an 8-year-old white girl was given a container of silicone putty at Christmas, 1950. She played with this frequently with no untoward reaction. In March, 1951, a vesicular eczematous reaction of both palms developed. The putty was the only unusual substance with which the child had been in frequent contact, and a patch test was applied to the forearm. When removed 48 hours later, a definite eczematous reaction was present. At this time the mother informed me that the putty seemed to pick up comic book print, lint from rugs, and other foreign matter.

The child was no longer allowed to handle the putty, and the condition cleared promptly in a few days.

A few weeks later, with the thought in mind that extraneous adherent matter and not the putty itself was the cause, the child was recalled to the office and a patch test made with a portion of freshly purchased material. When the result was read 48 hours later, there was no reaction at the site of the test.

Unfortunately the mother had discarded the original container, making it impossible to do a repeat test simultaneously with the fresh material.

The assumption, which I think can be justifiably made, is that during the course of handling foreign substances were incorporated into the putty, and the girl was sensitive to one of these. That it was not the dye used in coloring is obvious from the fact that the same colored preparation was used for the second test.

This case is reported because this substance, which is being used in physical medicine as well as in children's play, may absorb many sensitizing substances and may thus become a potential industrial, medical, or play-time hazard.

1001 St. Paul St. (2)

CONTACT DERMATITIS DUE TO N-ETHYL-O-CROTONOTOLUIDE OINTMENT (EURAX®)

EUGENE S. BERESTON, M.D.
BALTIMORE

In the past few years eurax® ointment containing 10% N-ethyl-o-crotonotoluide in a polyethylene glycol (carbowax®) base has been used as a scabicide and more recently as an antipruritic ointment. The literature reveals one report [1] of sensitization to the active ingredient and several instances of sensitization to the base.[2] Recently I observed a case of contact dermatitis from eurax® ointment which was due to the active principle, and because of the rarity of this finding I felt that it should be reported.

REPORT OF A CASE

M. C., the wife of a physician, had suffered from a pruritic recurrent eczema of the external auditory canals for many years. She had received various types of local therapy and considerable x-ray therapy in the past. During an exacerbation of her eczema, she applied curax® ointment to the external ears and to the skin around the ears for the itching. Within 24 hours, burning, itching, and swelling of these areas occurred and extended down the cheeks to the chin and anterior

1. Peck, S. M., and Michelfelder, T. J.: N-Ethyl-O-Crotonotoluide (Eurax) as an Antipruritic, New York J. Med. **50**:1934 (Aug. 15) 1950.

2. Couperus, M. J.: The Use of N-Ethyl-O-Crotonotoluide in the Treatment of Scabies and Various Pruritic Dermatoses, J. Invest. Dermat. **13**: 35 (July) 1949. Goldman, L.: Recent Advances in Chemical Control of Insects: A Brief Review Connecticut M. J. **13**: 624 (July) 1949.

neck. The next day she sought treatment, and examination disclosed an erythematous vesicular and edematous dermatitis of the external ears, cheeks, chin, and anterior upper neck. The dermatitis subsided in a week with cold compresses of 1 : 30 aluminum acetate and a simple lotion. Reaction to patch tests with eurax® ointment was 4+ within 48 hours. Patch tests with the ointment base and the active chemical of eurax® [3] elicited a 1+ reaction to the base in 48 hours and a negative reaction to the active chemical; however, a delayed 4+ reaction to the active chemical, with erythema and vesicle, appeared 24 hours after the patch test was removed.

CONCLUSIONS

A case of contact dermatitis due to N-ethyl-o-crotonotoluide (eurax®) ointment is reported.

Patch tests disclosed a 1+ reaction to ointment base in 48 hours and a 4+ reaction to the active chemical in 72 hours.

2406 Eutaw Pl.

3. Furnished through the cooperation of Geigy Company, Inc.

News and Comment

ANNOUNCEMENTS

The Department of Dermatology and Syphilology of New York University Post-Graduate Medical School (New York University-Bellevue Medical Center) announces that the second Sigmund Pollitzer Lecture will be given by Dr. Jerome W. Conn on Feb. 1, 1952, at 4 p. m. in the Main Lecture Hall of the College of Medicine, 477 First, Ave., New York. Dr. Conn is Professor of Medicine and Director of the Division of Endocrinology and Metabolism at the University of Michigan Medical School. The title of his talk will be "The Influence of Adrenal Cortical Activity upon the Electrolyte Composition of Thermal Sweat."

CORRECTION

In the article on "Evaluation of a New Drug for Topical Therapy of Tinea Capitis" by Doctors Edelson, Craster, and Haskin, with the technical assistance of Dr. Ignatoff, published in the Oct. issue of the ARCHIVES, page 444, Dr. Ignatoff's degree should have been given as D.S.C. rather than D.Sc.

Society Transactions

MANHATTAN DERMATOLOGIC SOCIETY

Paul E. Bechet, M.D., *President*

Isadore Rosen, M.D., *President*

George M. Lewis, M.D., *Secretary*

Dec. 12, 1950

Lymphoblastoma. Presented by DR. GEORGE M. LEWIS.

P. P., a woman aged 43, is presented from New York Hospital with a gradually enlarging, symptomless lesion on the forehead which has been present since Oct. 24. No skin defect, such as a nevus, was noted in this area.

The lesion is located on the medial aspect of the left side of the forehead. At present it is approximately 2.5 by 1.5 cm. and elevated about 0.75 cm. It is pinkish-red, well demarcated, and firm. There is no palpable lymphadenopathy.

The reaction to the serologic tests for syphilis were negative. A blood count in 1947 showed 6,500 white blood cells.

Biopsy showed, throughout the entire cutis and even fat, a diffuse infiltration of small round cells, wandering connective tissue cells, plasma cells, epithelioid cells, and eosinophilic leucocytes. There was a fine reticulum, some mitotic figures, and clumping of nuclei. Sarcoid and epithelioma could be ruled out. It is probably not a leukemia. The diagnosis was either mycosis fungoides or Hodgkin's disease.

DISCUSSION

DR. GEORGE C. ANDREWS: Could this pathologic picture not be caused by insect bites? Such lesions have been described. If it is mycosis fungoides d'emblee it can start anywhere, but it has not the clinical appearance of mycosis fungoides. It is simply a nodule, without any special shape or peculiar color. I have never seen mycosis fungoides d'emblee start without a bizarre lesion, and I would be a little skeptical of that diagnosis in spite of the histology, until more studies have been made. I think the possibility of insect bite should be strongly considered. As to treatment, I would be inclined to give a small dose of irradiation and keep the patient under close observation.

DR. WILBERT SACHS: Clinically, the peculiar waxy appearance suggests lymphadenosis cutis, but histologically this is not borne out. The clinical diagnosis of mycosis fungoides d'emblee on a single lesion is usually tentative. Hodgkin's disease may develop on the skin before it does internally. This has not been ruled out. There are not enough eosinophilic leucocytes and too many other cells for eosinophilic granuloma. This type of cellular reaction and the absence of abscess formation are not in favor of the diagnosis of insect bites. The nearest we can come to a diagnosis is Hodgkin's disease or mycosis fungoides d'emblee.

DR. GEORGE C. ANDREWS: Is it not true that some insect bites have been described as giving this picture?

DR. WILBERT SACHS: I think there are more foreign body giant cells, etc., than you see in this slide.

DR. PAUL M. CROSSLAND (by invitation): I recently heard of the new "imprint method" of studying the blood from a biopsy specimen. After taking the specimen it is cut in half with a clean, dry scalpel. The freshly cut surface is pressed and smeared on a glass slide. The slide is fixed and stained with Wright's stain. This method avoids the distortion of cells caused by the biopsy fixative solution. It is particularly appropriate for biopsies of the lymphoblastoma group, as it is claimed that stem cells, blast forms, Reed-Sternberg and multinucleated cells are more readily seen than in fixed tissue. It is further claimed that these cells can be found by this method when the peripheral blood picture is normal.

DR. WILBERT SACHS: That is true except in leukemia, in which the picture is quite definite. There are various types of cells that are not seen in the blood, as for example plasma cells.

DR. GEORGE M. LEWIS: The patient is considered to have lymphoblastoma, but the question of the exact type must be left for further study. The lesion has been present for only two months. The condition will probably become more typical as new lesions develop. The possibility raised by Dr. Andrews is interesting. It is apparent from our observation that this is a gradually expanding lesion. With insect bites the lesion does not increase in size. The plan is to administer x-rays in small dosage, perhaps 75 or 100 r, keeping the patient under close scrutiny.

Acrodermatitis Pustulosa Perstans and Psoriasis. Presented by DR. WILBERT SACHS and DR. PERRY M. SACHS.

J. D., a man aged 52, had psoriasis for many years. About one year ago he noticed an erythematous patch on the right sole. There were many vesicles and vesicopustules. Later another patch developed on the left heel. The lesions on the feet remain resistant to therapy. Repeated examinations have disclosed no fungi.

There are symmetric, scaly, erythematous patches on both forearms, the occipital region, the lower part of the sacrum, and over the knuckles. On the soles are seen erythematous scaly patches with small vesicles and vesicopustules.

Histopathologic examination of a lesion from the elbow revealed psoriasis, and from the right sole, acrodermatitis pustulosa perstans.

DISCUSSION

DR. GEORGE C. ANDREWS: Acrodermatitis pustulosa perstans is the same as acrodermatitis continua of Hallopeau. It starts first as a paronychial infection due to staphylococci and causes a persistent pustular exfoliative eruption of a digit or extremity. You can always culture staphylococci from it. It clears up, of course, with modern drugs. It is quite a different thing from this man's condition. He has no paronychia but a widespread eruption on the palms and soles. I think this comes from an internal cause, and frequently cultures from these pustules are sterile. I think the eruption would probably be cured by clearing up the focal infections which he obviously has.

DR. PAUL GROSS: It is true that the combination of pustular psoriasis of the palms and soles with typical psoriasis is rare but I would hesitate to speak of a combination of distinct entities. After all, we do know that pustular psoriasis may occur not only on the palms but in other locations. Just as bullous lichen planus and parapsoriasis varioliformis acuta are variants of the respective diseases, so is pustular psoriasis a variant of typical psoriasis. To accept the existence of pustular psoriasis does not rule out the recognition of the disease entity of pustular bacterid. This diagnosis has to be accepted in such conditions when the removal of the focal infection results in the complete and permanent cure of the eruption. I have convinced myself of this fact in several cases. The third disease which is frequently discussed in this connection is acrodermatitis suppurativa of Hallopeau which in its localized form may resemble pustular psoriasis. The disease in its localized and generalized form has so many distinctive features that it should be classified as an entity. I hope the name used by Dr. Sachs did not lead to misunderstanding.

DR. WILBERT SACHS: Do you agree that the patient has two diseases?

DR. GEORGE C. ANDREWS: Probably. I agree that there is such a thing as pustular psoriasis, although I think it is rare, and that many cases of so-called pustular psoriasis are something else, and that that diagnosis is made mostly for persons who do not have psoriasis at all. There is no reason why a psoriatic can not get pustular bacterid. I had a 75-year-old patient who had been under the care of Dr. Stokes and Dr. Howard Fox. They did allergy food tests and everything else except remove the tonsils. I saw her once only, had the tonsils out, and she was cured. I do not know why there is so much resistance to this concept. In every case I get an x-ray examination of the teeth. This man has nothing on the hands and feet that looks like psoriasis now. I think he has enough focal infection, obesity, etc., to have this id. As far as the white blood cell count goes, if it is now 10,000 I do not call it normal.

DR. ISADORE ROSEN: I agree that there is such an entity as pustular psoriasis. This patient has psoriasis; the lesions on the feet are typical of that disease. The erythema, the scales, and the extension of the erythema over the dorsal surface are often seen in patients with typical psoriasis involving the trunk.

DR. GEORGE M. LEWIS: I am not convinced that Dr. Sachs has proved his point, and in this case the fact that the man has psoriasis would be a point in favor of the condition being part of

that disease. I have had a few patients with lesions on the palms and soles in which there was some response to removal of foci of infection. I have many more patients, however, who have not responded to that treatment. We cannot distinguish clinically between pustular psoriasis and pustular bacterid, the only difference being that if the eruption disappears when you take the teeth out it is bacterid, and if not, the disease is pustular psoriasis. I think the point Dr. Gross brought out is interesting. I have independently arrived at the same conclusion. I do not see why we have to have so many names. Whether we call it pustular psoriasis or whatever you wish, it is a definite clinical entity. I think the onus of proof is still on those who would separate this from psoriasis, even though the pathology does not fit in with psoriasis, and even though some patients do get well with removal of foci of infection.

DR. ANTHONY C. CIPOLLARO: Those patients whom I have with this peculiar eruption do not happen to have infected teeth or tonsils. Usually the tonsils have been already removed, and the teeth are all right. They also have mild evidences of psoriasis elsewhere on the body, or it develops soon after. I just call it psoriasis, or pustular psoriasis, because that is a convenient term. I would like to cure it with antibiotics or by removing the teeth and tonsils, but I have not been successful as Dr. Andrews has.

DR. GEORGE C. ANDREWS: Perhaps when you study these cases you do not realize that tonsils can be bad even though they do not meet in the midline and there are no nodes. They can be foci of infection even though they are hidden behind the pillars. I always use a tonsil hook and pull them forward. Small embedded tonsils are often more harmful than very large ones. The reaction of tonsils to infection is much like that of the skin. Tonsils which are small, scarred, imbedded, and cryptic often harbor streptococci rather than staphylococci, and so on the skin you may get a local reaction to streptococci with a systemic reaction. I would like to make a test in this case. I do not promise he will get well, but I would ask Dr. Sachs to have those remaining teeth removed, for there is certainly a lot of infection around them; take out the tonsils, take off about 15 lb. (6.8 kg.) in weight and show him again after three months.

DR. GEORGE M. LEWIS: We have had three diseases mentioned: pustular psoriasis, pustular bacterid, and acrodermatitis pustulosa perstans. If there is no difference clinically or microscopically and they are the same disease, then what are we arguing about?

DR. GEORGE C. ANDREWS: Many of the patients with pustular bacterid have no signs of psoriasis, but have leucocytosis when groups of pustules appear. Clinically, there is a difference. This man had a lot of vesicles and an erythema around the pustules, which you do not find in pustular psoriasis. When you find more inflammatory reaction you are more likely to have a bacterid.

DR. WILBERT SACHS: I have very few patients with psoriasis and a pustular eruption on the palms and soles.

METROPOLITAN DERMATOLOGICAL SOCIETY OF LOS ANGELES

Henry Gordon Morgan, M.D., *President*

Harold C. Fishman, M.D., *Vice President*

Stanton B. May, M.D., *Secretary*

May 21, 1951

Chronic Discoid Lupus Erythematosus, Treated with Cortisone Topically. Presented by DR. IRVING A. LEWE.

Chronic Lupus Erythematosus Treated with Cortisone Ointment. Presented by DR. ROSE B. SAPERSTEIN.

DISCUSSION

DR. ERNEST T. FOX: It is obvious that these patients have improved. It has been my experience with an ointment of 25 mg. of cortisone per gram of base that there is considerable variation in the way patients respond to the treatment.

DR. HAROLD PRICE: The few patients that I have seen treated with cortisone topically have not impressed me greatly. I should like to ask Dr. Feldman what his experience with eventual

reaction to this treatment is, and whether any of the patients he studied have been controlled by the use of the base alone.

DR. FRED F. FELDMAN: Our period of investigation of the use of topical cortisone has now exceeded a period of nine months (Newman, B. A., and Feldman, F. F.: Effects of Topical Cortisone on Chronic Discoid Lupus Erythematosus and Necrobiosis Lipoidica Diabeticorum, *J. Invest. Dermat.*, to be published). Cortisone was used originally in our study in a concentration of 3.3 mg. and 5 mg. per gram of oil-in-water emulsion base ("neobase"). Shortly after instituting the study, polyethlene glycol (carbowax®) was substituted for the vehicle, and a concentration of 25 mg. per gram was used. Of 15 patients with chronic discoid lupus erythematosus studied, 4 showed complete clearing from topically administered cortisone alone. The remainder showed improvement ranging from 10 to 75%. In the majority of patients, maximum improvement did not occur until the concentration of cortisone was increased from 5 to 25 mg. per gram of ointment base. In no patient was there an untoward reaction, either locally or systemically. The tumid type of lesion appeared to respond better to topically administered cortisone than did the hyperkeratotic type. The first change noticed after topically administered cortisone was paling, followed by a reduction in the thickness of the lesion. In some patients the eruption took on a glazed appearance. In some instances healing occurred with pigmentation. Maximum improvement in all but one occurred within a period of one month after the use of cortisone ointment. If no improvement occurs after eight weeks of application of cortisone ointment, it is unlikely that any further change will be noted.

The most impressive results from topical use of cortisone occurred in necrobiosis lipoidica diabeticorum. Four patients showed rapid improvement, and in one there was complete healing.

No effect was seen in psoriasis, lichen planus, or granuloma annulare.

In answer to the question regarding controls with the base alone, we did not have a control group. However, in view of the recalcitrant response of both lupus erythematosus and necrobiosis to local treatment in the past, it appears unlikely that the base could play much of a role. Also, the fact that cortisone was effective in an oxycholesterol-petrolatum base (aquaphor®), an oil-in-water emulsion base ("neobase") and/or a polyethylene glycol (carbowax®) base, eliminates the ointment base as the important factor in the results. One of our patients with chronic discoid lupus erythematosus had no response to the control base but did respond to cortisone treatment.

DR. STANTON B. MAY: Has anyone injected cortisone or corticotropin (ACTH) into or just underneath the lesions; and would it be possible to administer cortisone into a lesion in liquid form with the hypospray®?

DR. FRED F. FELDMAN: In only two patients was cortisone injected into the lesions. No favorable effect was noted. I do not believe that treatment with hypospray® would be effective because cortisone is absorbed too rapidly into the blood stream with minimal concentration at the affected site. Application by iontophoresis might be worth trying if it were possible to make cortisone ionizable.

Lichen Nitidus. Presented by DR. FRED F. FELDMAN and DR. DAVID N. ALCON.
Case for Diagnosis: Junction Nevi? Presented by DR. L. F. SAVITT.
Acrodermatitis Continua (Dermatitis Repens?); Therapeutic Suggestions. Presented by DR. MEYER BERKE.
Dermatosis of Foot and Id Eruption of Hands. Presented by DR. ROSE B. SAPERSTEIN.
Dyshidrosis, Chronic, Recurrent, Left Hand; Lymphangitis, Chronic, Penis, with Elephantiasis. Presented by DR. ELIOT WOLK.
A Case for Diagnosis: Postherpetic Pigmentation and Neuralgia? Presented by DR. HERBERT A. FISHBEIN.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Paul Gross, M.D., *Chairman*

Anthony C. Cipollaro, M.D., *Secretary*

Oct. 3, 1950

A Case for Diagnosis: Multiple Erythematous Process: Drug Eruption? Psoriasis?

Presented by DR. GEORGE M. LEWIS.

W. C., a Negro aged 47, a native of Trinidad, until recently a laboratory assistant in parasitology, experienced a sudden onset of pruritus in June, accompanied with a widespread eruption of punctate, erythematous, scaly papules. Initial treatment by a physician consisted of one

injection of penicillin and application of calamine lotion. When he was first seen at New York Hospital, the differential diagnoses were rupial syphilid, psoriasiform syphilid, psoriasis guttata, or drug eruption. Drug ingestion was denied. The patient continued to feel well aside from the pruritus, but the individual lesions increased in diameter while new lesions developed in all areas. A complete physical examination failed to reveal any significant abnormalities, and the reactions to a battery of serologic tests for syphilis were repeatedly negative. He was treated topically with a mild tar.

Early in August the patient reported improvement in the itching but experienced unexplained bouts of fever. The skin lesions progressed to the point of coalescence, and the fingernails began to be involved. Pain developed in the right metatarsophalangeal joint, and this was followed in early September by soreness and pain in the right hip. There was no evidence of conjunctivitis or urethritis. In place of the tar, an oxycholesterol-petrolatum ointment (aquaphor®) and water were used. There was a slight loss in weight.

The past history included gonorrheal urethritis in 1932, treated and cured with "herbs," without sequelae. In 1945 a positive reaction to serologic test for syphilis was elicited, without history of primary or secondary syphilis. He was treated weekly for nine months with arm and hip injections. The reaction to serologic tests have been negative for syphilis since completion of treatment.

Initially the lesions were generalized but discrete, appearing as heavily scaled papules and nodules. In the interim these have flattened out and enlarged to their present state of coalescence. Scaling persists but is not so pronounced. Erythema has increased. The palms and soles remain uninvolved.

Urologic examination was normal aside from median bar, slight lateral lobe hypertrophy, and changes in the prostatic urethra suggestive of long-standing infection. Prostatic secretion was unobtainable.

Results of urinalyses were as follows: On Aug. 2 sugar was 1+; red blood cells, 8 to 10 per high power field, and there were many white blood cells. On Aug. 9 a trace of albumin and many white blood cells were found. On Sept. 25 the urine was turbid; there was a faint trace of albumin and occasional white blood cells; urates were 4+. A roentgenogram of the chest was normal, as was a flat roentgenogram of the abdomen.

Biopsy showed the vessels of the upper cutis to be dilated, and there was a moderate and diffuse infiltration of small round cells and wandering connective tissue cells. There was considerable interstitial edema of the upper cutis. The epidermis was irregularly acanthotic. The palisade layer was intact and contained considerable pigment. The suprapapillary plates were thick, and most of the granular layer was retained. There was some parakeratosis. The diagnosis was multiple erythematous process, probably drug eruption; there was no evidence of syphilis or mycosis fungoides.

DISCUSSION

DR. MAURICE J. COSTELLO: I think if I had to make one diagnosis I would choose psoriasis, although there are features of other dermatoses. In Negroes psoriasis may take on a somewhat different form than in white persons.

DR. MAX SCHEER: It seemed to me as though there were slight induration of the borders of some lesions, especially some of the sharply demarcated lesions on the lower aspect of the left forearm. It is true that findings from histologic examination were normal, but biopsy was done from one very small area of an extensive eruption, and if another area were examined, particularly an infiltration, it might show a different picture.

DR. WILBERT SACHS: At first the clinical diagnosis was a drug eruption. Later the eruption changed, suggesting psoriasis, syphilis, mycosis fungoides, etc. Two pieces of tissue were taken from two different areas, and they showed no evidence of syphilis, psoriasis, or mycosis fungoides. All we could say was multiple erythema. It looks very much like mycosis fungoides now.

DR. LOUIS TULIPAN: I think clinically it is erythema figuratum perstans. The lesions are well-circumscribed patches with a scaly center and slightly raised red border, which fits in with that disease.

DR. DAVID BLOOM: In eczematous lichenoid eruptions in Negro patients these circumscribed, hyperpigmented, somewhat-raised plaques are frequently seen. I agree with Dr. Scheer that the sharply outlined lesions on the hands force consideration of mycosis fungoides.

DR. CHARLES WOLF: Today we see an acute inflammatory process which is going through an evolutionary phase. It is rather early, or perhaps impossible, to make a definite diagnosis. If it is a drug eruption, it should have improved by this time. The patient is a porter and is exposed to fumes and contactants. Therefore, we have to consider dermatitis venenata superimposed upon another disease. There is a remote resemblance to granuloma fungoides. The lesions are infiltrated, sharply demarcated, and pruritic. There is always an early stage of granuloma fungoides, but to have it evolve to such a degree in so short a time would be unusual. Granuloma fungoides d'emblee is fulminating, with the tumor stage appearing first, but this is not that type. Blood and bone marrow studies should be performed and the case presented again at a later date.

DR. GEORGE M. LEWIS: It is reassuring to hear the varied opinions, because we had the same type of discussion at our staff conference. The lesions as seen tonight suggest psoriasis perhaps more than any other dermatosis. The process appears to be in a stage of evolution, and there would appear to be a grave possibility of exfoliative dermatitis as a complication. We have used soothing topical remedies only, so overtreatment cannot account for any of the clinical findings. In considering the basic or fundamental disease, mycosis fungoides has been considered, although there is no histologic confirmation at this time.

A Case for Diagnosis: Granuloma of the Nose? Tertiary Syphilid, Treatment Resistant? Presented by DR. GEORGE M. LEWIS.

C. V., a man aged 73, presented himself at Memorial Center for Cancer and Allied Diseases in March, 1941, with a lesion below the bridge of the nose, 2.5 by 2 cm. in size, of four or five years' duration. There were no symptoms other than itching at the margins of the lesion. From the beginning it appeared slightly discolored; it had not ulcerated, and the patient felt the rate of growth was increasing. It was noted on the original examination that the nasal passages were distorted and that a good portion of the nasal septum had been removed or destroyed. The patient reported that he had had several operations for nasal obstruction.

The patient had a chancre at the age of 20, with no treatment until 1938 when he received sporadic antisyphilitic therapy from Metropolitan Hospital. The reactions to serologic tests for syphilis were repeatedly negative.

On the suspicion of epithelioma, the lesion was excised down to the cartilage and replaced with a full-thickness skin graft. A definite histologic diagnosis could not be made, but gumma was suggested. Weekly injections of neoarsphenamine, totaling 13, were administered between September, 1941, and January, 1942, followed by four injections of bismuth. In November, a recurrence of the original process was noted at the right of the skin graft.

Biopsy revealed only "granulomatous inflammation."

Both areas of evident recurrence were then treated with 500 r of unfiltered, low-voltage x-rays for two weeks in September, 1943. It was felt that improvement resulted, so the same dosage was repeated in October. Difficulty in breathing through the nose, especially on the right side, continued.

Roentgenograms in January, 1944, demonstrated increase of the destructive nasal process. The Board of Health reported the reaction to the Wassermann test for syphilis to be repeatedly negative, but following two injections of bismuth the lesions were said to have improved. Further antisyphilitic treatment was administered for an unknown period, with slight regression of the process involving the nasal skin. In January, 1946, it was felt that the lesion in the skin of the nose was larger and more purple than formerly. An enlarged heart was found with apical diastolic murmurs and aortic regurgitation and stenosis. Further antisyphilitic therapy by the Board of Health was advised. Potassium iodide was begun in November, 1947, and continued until March, 1948. The patient felt this improved the nasal lesion and decreased the intensity of its color. In May, 1949, the process had gradually advanced toward the inner canthus of the right eye. Biopsy reported a "chronic inflammation with marked eosinophilia." Penicillin therapy, presumably in antisyphilitic doses, was administered in August, 1949, with total dosage unknown. No subsequent improvement was evident. In February, 1950, the granulomatous process had spread along the right infraorbital skin. Penicillin, 600,000 units a day for 10 days, was administered in June, and by September the lesion was somewhat softer and less intensely red.

In February, 1950, smears and cultures were negative for acid-fast bacilli. Biopsy at that time revealed a "granulomatous lesion with marked endarteritis suggesting tertiary syphilid."

DISCUSSION

DR. LOUIS CHARGIN: The infiltration present does not resemble any form of syphilis with which I am acquainted. In due time there may develop a manifestation which may make it possible to arrive at a definite diagnosis, which I doubt will prove to be syphilis.

DR. MAURICE J. COSTELLO: This patient reminded me strikingly of one whose case I reported in 1941 before the American Medical Association, a woman who ended with this type of deformity. She was also thought to have had syphilis, but it proved to be a pyogenic destruction of the nose by the microaerophilic hemolytic Streptococcus. If any activity remains, organisms should be looked for and the patient treated as my patient was successfully treated, with medicinal zinc peroxide paste.

DR. BEATRICE M. KESTEN: I would not be able to offer a diagnosis, but I wager it rests between infection, a malignant lesion, or sarcoid. The bony destruction of the face tends to rule out sarcoid. I would suggest another biopsy and also bacterial studies.

DR. WILBERT SACHS: We took a biopsy specimen rather recently and I also saw the previous one. Our diagnosis was granuloma, but we did not know the type. The histologic picture ruled out tuberculosis and leprosy, but we felt that syphilis was a possibility.

DR. GEORGE M. LEWIS: This patient gives a confused and contradictory history. The suggestion of another biopsy is good in that negative information is never sure, and the previous histologic data gave little positive help.

Nevoxanthoendothelioma. Presented by DR. ANTHONY C. CIPOLLARO.

W. L., a one-year-old boy, manifested discrete lesions on the thorax and shoulders nine months ago. This was followed by a quick succession of similar lesions on the scalp and other portions of the body. The patient was seen by a local physician one month after the onset; biopsy was performed, and blood studies were made. Five months after the onset, the patient was seen in the Dermatology Clinic of New York Hospital. The only positive findings in the history were hay fever in a paternal relative and an angioma on the forehead at birth.

Numerous discrete, yellow, lentil- to larger-sized, slightly erythematous lesions are present on the scalp, face, neck, trunk, and extremities.

The blood cholesterol was 166.

Biopsy showed a slightly hyperkeratotic, compressed epidermis consisting of only a few layers of cells. The corium was densely infiltrated, showing a large number of histiocytes. Foam cells were present but no giant cells. The capillaries showed endothelial proliferation. The impression was (1) nevoxanthoendothelioma; (2) xanthoma.

Since the diagnosis of nevoxanthoma does not usually impart a serious prognosis, and since spontaneous remission is most likely, no treatment was instituted. The child is being followed from time to time with examination and blood chemistry studies.

DISCUSSION

DR. WILBERT SACHS: I believe clinically it is a classic case of nevoxanthoendothelioma. It will probably clear up in one or two years without treatment.

DR. MAURICE J. COSTELLO: I cannot discuss the case from the histologic point of view, but could this not be called xanthoma tuberosum? Patients with nevoxanthoendothelioma have one or two lesions, not many; oftentimes a halo develops around the lesion, sometimes intense enough to produce vesiculation. The reason the mother brings the child to a physician is often because of the halo. There may not be elevation of the blood cholesterol. From the clinical point of view, this impressed me as xanthoma tuberosum. The child had some lesions on the elbows.

DR. DAVID BLOOM: This is a typical case of so-called nevoxanthoendothelioma. The distinction from xanthoma tuberosum is important particularly because of the prognosis. The differential diagnosis is made first, by the cholesterol content of the blood which is normal in nevoxanthoendothelioma, and increased in xanthoma tuberosum, second, by the location of the lesions, which most frequently occupy areas of pressure in xanthoma tuberosum. A third point is that xanthoma tuberosum is hereditary.

DR. WILBERT SACHS: Dr. Costello brings up an interesting question. Microscopically, we sometimes have difficulty distinguishing between xanthoma and nevoxanthoendothelioma. For instance, in xanthoma tuberosum you should get only foam cells. Occasionally in nevoxanthoendothelioma one finds nevus cells, which are not seen in xanthoma. I do not depend so much on the cholesterol in the blood, because it may be normal. The only thing we can depend upon is time. If this patient has a spontaneous remission we have to assume it was nevoxanthoendothelioma and not xanthoma tuberosum. In either case I would say to leave the lesions alone and not treat them. If it is xanthoma tuberosum, treatment is not going to help; and if it is nevoxanthoendothelioma, it will disappear.

DR. DAVID BLOOM: Xanthoma tuberosum is, as far as I know, always associated with hypercholesterolemia. In fact, it is realized and accepted now that the essential primary factor in this disease is hypercholesterolemia and that involvement of the skin is secondary. Instead of the term xanthoma tuberosum, it should be called "essential familial hypercholesterolemia," as Wilkinson has suggested (*Bull. New York Acad. Med.* **26**:670 [Oct.] 1950).

DR. ANTHONY C. CIPOLLARO: All essential points regarding differential diagnosis have already been taken up. I think both clinically and histologically this child's lesions fit in with the concept of nevoxanthoendothelioma. Acknowledging the fact that xanthoma tuberosum multiplex and nevoxanthoendothelioma have characteristics in common, I think the differential points have been well covered. I will go along with the latter diagnosis, with leaving the child untreated, and in disagreeing with Dr. Bloom that in nevoxanthoendothelioma the blood cholesterol is well within normal limits.

A Case for Diagnosis: Fibrosarcoma? Presented by DR. GEORGE M. LEWIS.

P. McK., a man aged 52, was first seen in the dermatology clinic of New York Hospital in August, 1944, complaining of an asymptomatic lesion on the abdominal wall which was first noted in 1940. He revisited the clinic today, stating that a large tender, painful lesion had appeared on the right side of the abdominal wall within the past seven days. He is in good health otherwise and has had no weight loss.

Reddish, asymptomatic, firm, nodular cutaneous lesions are present in the midline above the umbilical region. From these lesions an indurated subcutaneous band, approximately 10 cm. in length and 3.5 cm. in width, extends to the right upper quadrant. At the distal portion is a subcutaneous firm, tender, spherical mass, approximately 3.5 cm. in diameter.

A blood count on Oct. 3, 1950, showed 12,600 white blood cells, with lymphocytes, 26, a few (rare) very young; monocytes, 6; eosinophils, 6; and polymorphonuclear leucocytes, 40 (mature) and 22 (band form). The platelets were normal.

Biopsy performed on Sept. 20, 1944, showed a fairly normal epidermis just beneath which was a tumor mass involving sweat glands in interlacing bands of fibrous tissue, alternating with cords of cells which stained pink with the Masson stain and had some resemblance to nerve trunks. The general appearance of the specimen indicated that it was a subcutaneous neurogenous fibroma, in no way malignant.

DISCUSSION

DR. JOSEPH J. ELLER: If this lesion is a fibrosarcoma, the treatment should be surgical and not by x-rays or radium.

DR. MAX SCHEER: I think this falls into the group of cases described by Darier which he called dermatofibrosarcoma, later described by Erich Hoffman. The characteristic lesion is a tumor in the abdominal wall, which is only locally malignant. If the tumor is excised adequately, there is no recurrence; but if it is not removed widely enough, sooner or later there is a recurrence. They do not metastasize ordinarily, although a few instances have been reported.

DR. ERICH KUZNITZKY (by invitation): In my opinion this is dermatofibrosarcoma protuberans. It was decided first by Grabisch and me, and later by Darier, and E. Hoffman finally gave it its present name. I think it is a hamartoma: It does not metastasize and often undergoes myxomatous changes.

DR. FREDERICK REISS: I agree only partially with Dr. Kuznitzky. I do not see any protuberance in this case. Those described by Darier were keloidal in nature and very protuberant. The histologic picture, however, is in favor of the diagnosis.

DR. GEORGE M. LEWIS: This type of tumor has little tendency to progress in virulence, and the original lesion was treated six years ago. Our pathologist, Dr. Chandler Foote, considered the lesion to be a neurofibroma, and for that reason only part of it was removed. It is evident that the patient's history of one week's duration for the mass present tonight is erroneous. Dr. Sachs mentioned that there may be a change in the type of tumor now present.

Intraepidermic Nevus. Presented by DR. WILBERT SACHS.

D. L., a girl aged 16, was first seen in the New York Hospital Dermatology Clinic on Aug. 18, 1950, with a growth on the scalp of nine years' duration. According to the mother, the site of this lesion has been hairless from birth. It was smooth until nine years ago when a small, hard, slowly enlarging growth was noted. This was removed by electric needle two and one-half years ago by a local physician. Six months after this treatment a group of small, firm tumors appeared near the spot where the old one was removed. These have been growing in size and number. There is some evidence of a tendency to keloid formation in former injuries which will influence selection of the mode of therapy of the scalp lesion.

In the left posterior portion of the scalp there is a hairless area about 2 by 3 cm. in dimension, in which a slightly raised, pinkish plaque is evident. At its edges are seen soft, wart-like papillomatous excrescences extending out from the hairless area. There are no symptoms. The forehead has many small, slightly raised nodules under the skin, 1 by 1 mm. in size, and also at the hairline over the temporal region.

Biopsy showed a loosely woven hyperkeratotic keratin layer overlying a moderately irregularly acanthotic epidermis which tended to be thrown into upward projecting folds. In some areas of the epidermis were what appeared to be uniformly arranged masses of nevoid cells. Inflammatory reaction was lacking in the cutis. The pathologic diagnosis was intraepidermic nevus.

DISCUSSION

DR. JOSEPH J. ELLER: I recommend that the lesion be left untreated, first, because it is benign, and second, because, being brownish, it is hardly noticeable through the hair and certainly less so than a whitish, bald area would be following removal of the lesion.

DR. MAURICE J. COSTELLO: I wonder if Dr. Sachs feels absolutely sure that it is a verrucous nevus? The location is a common one for a minor ectodermal defect. There is a moist bald spot which heals, and then I surmise that it took on a verrucous appearance because of irritation.

DR. WILBERT SACHS: In regard to the history of a bald spot, I believe part of the area may be due to treatment by a local physician. The lesion is an epidermic nevus, which is a type of ectodermal defect. The reason for presenting the patient is the question of treatment. When the lesion is small, therapy is not too difficult; when it is large, eradication is not a simple matter, and I agree with Dr. Eller that this lesion should not be treated unless the patient insists.

Pityriasis Lichenoides Chronica (Parapsoriasis). Presented by DR. MARGARET KLUMPP.
Parapsoriasis en Plaque. Presented by DR. MARGARET KLUMPP.
A Case for Diagnosis: Pemphigus? Presented by DR. GEORGE M. LEWIS.
Poikiloderma Atrophicans Vasculare (Jacobi). Presented by DR. ANTHONY C. CIPOLLARO.
Lichen Sclerosus et Atrophicus. Presented by DR. WILBERT SACHS.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Edward F. Corson, M.D., *Chairman*

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Oct. 20, 1950

Multiple Benign Cystic Epithelioma. Presented by DR. VAUGHN C. GARNER.

W. D., a white boy, aged 10 years, with a bony deformity of the right chest wall, presents a great profusion (400 to 500) of small, pigmented, pedunculated, and sessile papules, especially around the neck, shoulders, and sides of the chest, the latest crop developing over the abdominal wall. A score or more of miliary pearly papules are evident about the eyelids, which clinically are typical of acanthoma adenoides cysticum. Many of the lesions over the neck and upper

torso resemble the cutaneous tags of the neck so commonly seen in women. The lesions began when the patient was 5 years old. He has one sibling, who is unaffected.

The report on the biopsy specimens from three lesions, clipped flush with the skin from the neck and chest, was as follows: "These were pedunculated lesions containing islands of basophilic-staining epithelial cells in the corium. The surface was fairly smooth and the stratum corneum was normal. The granular layer was intact. The prickle-cell layer was thin and flattened, and the basal layer was intact. Throughout the corium were round and stellate islands of pigmented, basophilic-stained epithelial cells. In the center of many of these islands there were cysts containing a homogeneous pink material resembling keratin, while at the periphery of the islands the cells were densely packed and had a palisade arrangement. Some of the cysts were packed with pigment and were surrounded by two to four layers of flat cells. About the islands of cells the collagen was edematous and loosely packed, and in some places intracellular and extracellular pigment was seen."

DISCUSSION

DR. MEYER L. NIEDELMAN: Clinically the lesions look more like ordinary small, pigmented type of papilloma. If it is multiple benign cystic epithelioma, I think electrodesiccation would be the simplest procedure.

DR. HERMAN BEERMAN: I feel responsible for that diagnosis, having studied three of the lesions, all of the type you saw tonight; and Dr. Wiedman also examined the sections from this patient.

DR. H. H. PERLMAN: What accounts for the increase of pigment cells? Is there an increase of melanin?

DR. FRED D. WEIDMAN: The sections do not show the usual kind of cystic change of multiple benign cystic epithelioma, but basal-cell carcinoma of the pigmented variety. Pigmented basal-cell cancers are common indeed. That, though, is not opposed to the possibility of its still being multiple benign cystic epithelioma. Dr. Beerman recalls the work that Goldman did on seven patients in three generations of the same family, and, as Mallory pointed out a long time ago, many of the ordinary basal cell cancers have the same kind of origin as the cystic examples which characterize multiple benign cystic epithelioma; that is, they are primary epithelial germ tumors, such as Lever has described. Some of them remain of basal cell type, as here, although in this particular case there is a certain trichoepitheliomatous structure. That, too, may or may not undergo cystic change, but that is neither here nor there, so far as the basic principles are concerned. In this patient I think it is a salvation that there is this particular distribution around the eyes. I grant that it is not seen at the corners of the nose and in the middle of the chin in the typical manner, but in view of the work of Mallory and Goldman and many others, this case can be fitted into multiple benign cystic epithelioma. I admit that clinically, and to a certain extent histologically, it is atypical.

DR. J. P. GUEQUIERRE: In this patient I saw typical cystic lesions, but I never saw multiple benign cystic epithelioma with pedunculated lesions. They looked to me more like small pedunculated nevi, more like pigmented skin tags. How do you account for that, Dr. Weidman?

DR. FRED D. WEIDMAN: I cannot, except that one is dealing here with a congenital abnormality. The latter are subject to vagaries.

DR. JAMES M. FLOOD, Sayre, Pa.: I should like to suggest the use of liquid nitrogen administered on very fine wisps of cotton on the end of an applicator. The lesions would freeze almost immediately and in about three to six days fall off.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: Why not try the new combination recently developed of 25% podophyllum and 25% salicylic acid in alcohol and acetone, equal parts?

Localized Xeroderma Pigmentosum. Presented by DR. JOSEPH F. RICCHIUTI, Pottsville, Pa.

J. B. M., a white man, aged 26, presents on the nose numerous scaly, brownish nodules about 0.5 cm. in diameter. There is atrophy of the skin about the nose and cheeks. Many follicles are dilated. A few whitish scars are visible. There are also a few reddish-brown nodules on the right cheek. The eruption was first noted on the face at the age of 3 months. Over the years it has gradually involved the nose. Five epitheliomata have been removed from the face.

The patient was operated on for pterygium in 1937 and had a mastoidectomy in 1944. Two siblings are also affected in the same way. The parents are not related. The report on the biopsy specimen was "xeroderma pigmentosum and epitheliomata."

DISCUSSION

DR. JOSEPH F. RICCHIUTI: I have been observing this boy for ten years, and he seems to be getting better; the disease is less severe and is fairly well localized to the nose and cheeks. He has had five epitheliomas destroyed in that time.

DR. FRED D. WEIDMAN: Were these basal or squamous cell cancers? I recall that Dr. Schamberg once showed three siblings at one meeting of this Society, and in two the cancer was squamous, which is to be expected, but the other was basal. I am curious to know whether, in one and the same patient, all are of one kind or whether some at one time are basal and some squamous. It is very seldom that one sees a localized xeroderma pigmentosum.

DR. JOSEPH F. RICCHIUTI: This boy had five lesions removed; two from the nose were basal cell, and the lesion on the lower lip looked like the squamous cell cancer seen in older men. The one on the back was basal cell.

Dermatomyositis in an 8-Year-Old Boy. Presented by DR. EDWARD F. CORSON and (by invitation) DR. S. E. RYNES.

FOLLOW-UP NOTE: Following treatment with corticotropin (ACTH) (total dose, 940 mg.) and cortisone (2,000 mg.) the rash had almost disappeared. Some muscular pains, particularly around the knees, were still present. Since the discontinuance of cortisone, the boy has received pregnenolone orally and *p*-aminobenzoic acid.

Mycosis Fungoides with Tumor of the Lip. Presented by DR. HENRY B. DECKER and (by invitation) DR. J. K. CORSON.

Acne Keloid. Presented by DR. JOHN M. SIEGEL, Allentown, Pa.

Vascular Nevus. Presented by DR. GEORGE E. PFAHLER and DR. ROBERT APPLESTEIN.

Edward F. Corson, M.D., *Chairman*

H. E. Twining, M.D., *Secretary*

Feb. 16, 1951

Multiple Epitheliomatosis; Arsenical Keratoses of the Palms and Soles. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

A. K., a white man aged 58, thin, poorly nourished, with retarded mental reactions, presents numerous palmar and plantar hyperkeratotic circumscribed lesions. Over the trunk and extremities are scattered lesions varying from simple hyperkeratoses to verrucous nodular plaques and atrophic scars with telangiectatic surfaces on the peripheries. They have been present for an indeterminate number of years. The patient was treated many years ago with arsenic by mouth. Since 1940 innumerable cutaneous lesions have been surgically excised, electrodesiccated, and irradiated in the radium clinic at the Philadelphia General Hospital. The patient burned his right hand in 1946 and had a skin graft. The previous medication for epilepsy consisted of bromides. He has recently been treated with diphenylhydantoin (dilantin®) sodium and phenobarbital sodium. He has had epilepsy since the age of 16 and has had five hospital admissions for postepileptic injuries, burns, and contusions.

DISCUSSION

DR. CARROLL S. WRIGHT: A great mistake is made in some of these patients in not using either solid carbon dioxide or dry ice. This man already shows a great deal of radiodermatitis. One cannot injure a patient with solid carbon dioxide or dry ice, and he can frequently be cured with one treatment, 40 to 60 seconds' application at the time; at the end of a week there is slough, and at the end of four to six weeks healing is complete. It cannot be employed in this particular patient; he has too many lesions. It is not the treatment of choice in these patients.

DR. EDWARD F. CORSON: How about liquid nitrogen, Dr. Flood?

DR. JAMES M. FLOOD, Sayre, Pa.: If solid carbon dioxide will work, liquid nitrogen is also indicated.

DR. DONALD M. PILLSBURY: We have been treating a number of similar patients with grenz rays a little above the usual voltage, 15 kv., and the results to date have been extremely good. I do not know whether these patients will have any recurrences or not; they may. We treated the first about a year ago. The lesions disappear quite rapidly when treated with 1,500 to 2,000 r, unfiltered, at 15 kv.

Symbiotic Bacterial Infection and Gangrene of the Skin. Resistant to Antibiotics and Healed Following Excision and Graft. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. HAROLD E. PIERCE.

Psoriasis(?); Possible Atopic Dermatitis(?). Presented by DR. H. H. PERLMAN and (by invitation) DR. P. P. WESTFALL.

Epidermolysis Bullosa, Congenital. Presented by DR. MARJORY K. HARDY, (by invitation) DR. B. A. GROSS, and (by invitation) DR. LOUIS HOFFSTEIN.

Premycotic Phase of Mycosis Fungoides(?); Generalized Neurodermatitis(?). Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Granuloma Annulare(?); Leukemid(?). Presented by DR. JOHN P. SCULLY.

A Case for Diagnosis: Lupus Erythematosus? Presented by DR. MARJORY K. HARDY and (by invitation) DR. LOUIS D. HOFFSTEIN.

Epidermolysis Bullosa; Pulmonary and Lymphnode Tuberculosis. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Kaposi's Hemorrhagic Sarcoma (Treated); Small Recurrence of Stump Auricular Fibrillation with Left Hemiplegia. Iridoschisis of the Left Eye. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Lichen Planus Hypertrophicus. Prurigo? Lichen Amyloidosis? Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Chronic Osteomyelitis. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Psoriasis. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Arthritis, Rheumatoid. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Exfoliative Dermatitis. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Scleroderma (Scleredema?). Presented by DR. HAROLD E. PIERCE and (by invitation) DR. LOUIS D. HOFFSTEIN.

Lymphoblastoma. Rheumatoid Arthritis. Presented by DR. CARMEN C. THOMAS.

Pemphigus Erythematodes? Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Lupus Erythematosus, Discoid? Multiple Peripheral Neuropathies (Arsenical? Due to Intrinsic Unknown Disease?). Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Pemphigus Vulgaris Having Its Onset in Atrophic Vulvar Mucous Membrane. Presented by DR. CARMEN C. THOMAS and (by invitation) DR. LOUIS D. HOFFSTEIN.

Fox-Fordyce Disease. Presented by DR. HAROLD E. PIERCE and (by invitation) DR. LOUIS D. HOFFSTEIN.

Spontaneous Keloids. Hypertensive Cardiovascular Disease. Obesity. Presented by DR. BERNARD L. KAHN and (by invitation) DR. LOUIS D. HOFFSTEIN.

Dermatitis Venenata (Crayons?). Presented by DR. H. H. PERLMAN, (by invitation) DR. P. P. WESTFALL, and (by invitation) DR. J. GROPEN.

Mild Type of Keratosis Palmaris et Plantaris. Presented by DR. H. H. PERLMAN, (by invitation) DR. P. P. WESTFALL, and (by invitation) DR. J. GROPEN.

Edward F. Corson, M.D., *Chairman*

H. E. Twining, M.D., *Secretary*

March 16, 1951

A Case for Diagnosis: Atypical (Vesicular) Pityriasis Rosea? Dermatophytid? Drug Eruption? Presented by DR. H. E. TWINING, DR. CARROLL F. BURGOON, and (by invitation) DR. LOUIS JAFFE.

Y. C., a Negro girl, aged 14, has an acneform eruption on the face. There is a crusted, oozing, excoriated patch on the anterior surface of the left ankle, about ¾ in. (1.9 cm.) in diameter, with hyperpigmentation but no induration of the border. There is a similar excoriated, oozing patch about ⅜ in. (0.95 cm.) in diameter and surrounded by an erythematous halo on the left thigh. These are initial lesions. There is an eruption consisting of elevated papules and elevated oval plaques, ranging in size up to about 1 in. (2.5 cm.) in length, with their long axes in the lines of skin cleavage, most prominent over the trunk, arms, neck, and thighs, but also involving the forearms, with a few scattered lesions on the face and the dorsa of the hands. Most of the oval plaques exhibit crusted centers, with narrow, scaly borders. Most of the larger lesions exhibit an erythematous areola and marked pustulation on their borders. On the buccal mucosae, opposite the line of occlusion of the teeth there are two whitish patches. The patient has had the acneform eruption on the face for a year. About one and one-half weeks ago she noted a "sore" on her left ankle and one on the left thigh. She is vague as to the initial appearance of these lesions. About three days later a generalized eruption developed accompanied by moderate itching. She was seen in the accident ward a week ago (March 9) and was given penicillin. She applied a medicated salve and soap ("Sayman's healing salve" and "Sayman's

vegetable wonder soap") without effect. She was first seen in the dermatologic clinic on the morning of this presentation, March 16. The reactions to serologic tests for syphilis on April 19, 1950, and March 16, 1951, were negative. The results of the dark-field examination of the lesion on the arm were normal on March 16, 1951.

DISCUSSION

DR. BERNARD L. KAHN: I think it is an atypical staphylococcosis or just a pyoderma.

DR. A. STRAUSS: I think it is varicella.

DR. CARROLL F. BURGOON: We did not think of varicella this morning. This evening a smear was examined, and there are no multinuclear giant cells such as are seen in varicella. So, on that basis, I think we are safe in saying this is not chickenpox.

DR. DONALD M. PILLSBURY: I have seen four patients recently with this condition. The lesions look almost like nummular eczema. In one of our patients we were able to follow the entire course of the disease, and she recovered completely. I believe she has an eczematous type of pityriasis rosea.

DR. HERBERT J. SMITH: I think it is pityriasis rosea.

DR. THOMAS BUTTERWORTH, Reading: I would diagnose this as a pityriasis-rosea-like drug eruption. I have seen only three patients with pityriasis rosea vesiculata, and in every instance the primary lesion was a papulosquamous one surmounted by a vesicle, and did not resemble this at all. I have observed a number of patients who had conditions similar to this following bismuth therapy, in which one sees pityriasis-rosea-like eruption with considerable moisture in the lesions.

DR. H. E. TWINING: This is the second case that we have seen with vesicular lesions. Yesterday, at the United States Naval Hospital, a patient was observed with typical lesions of pityriasis rosea on the trunk and vesicles on the palms and soles.

Erythromelalgia(?); Thromboangiitis Obliterans(?). Presented by DR. H. E. TWINING.

W. L., a white man, aged 38, complains of tenseness, burning, and swelling of the radial half of the right palm, the thumb, index, and middle fingers, the ulnar half of the left hand, and the little and ring fingers. The erythema subsides in 7 to 10 days and is followed by considerable desquamation. To date there have been three similar attacks, with complete remissions. The color during the attack is not altered by a change in position. A sharp line of demarcation separates the normal from the involved area. About one year ago an intense redness developed, with swelling of the radial half of the right palm, the thumb, and the index and middle fingers; while the ulnar side of the left hand, together with the little and ring fingers, was involved.

For the past four or five years the patient has been treated for arteriosclerosis; the medication is not known.

The blood counts and urinalysis were within normal limits. The reaction to the Kahn test was negative for syphilis.

The patient has been treated with aluminum acetate and boric acid compresses, followed by a zinc oxide and boric acid ointment.

Tattoo, with Reaction to Cinnabar. Presented by LT. J. F. MORRELL (MC), U.S.N., (by invitation), from the service of CAPT. ROBERT L. GILMAN (MC), U.S.N.

A. L., a white man, aged 20, was tattooed on the left arm in 1949. Five months later the red-pigmented areas became elevated. This subsided for about a month, and once again the area became elevated and has persisted. The red parts are raised, firm, scaly, and nontender. The patient recalls that ammoniated mercury ointment applied to burns caused additional irritation

The routine laboratory tests were within normal limits.

The report on the biopsy specimen was as follows: "tattoo with reactive acanthosis, hyperkeratosis, and chronic inflammation."

Patch test with ammoniated mercury ointment, 5%, on the right forearm, elicited a strongly positive reaction.

DISCUSSION

DR. MEYER L. NIEDELMAN: This is the first case I have seen with so many lesions due to a foreign-body reaction to mercury. It is interesting to note that only the areas which have the

cinnabar have reacted. At first glance one would think these were scars or keloids. I have under my care at present a young man who is tattooed from his wrists to his shoulders. Of the various methods tried, including tannic acid scarification, the best results have been obtained with procaine anesthesia and electrosurgery. No skin grafts are necessary, as spontaneous healing occurs readily, especially when the newer antibiotic ointments are used.

DR. DONALD M. PILLSBURY: It was not suggested that these lesions are keloids. They are frankly an inflammatory reaction to cinnabar. Has dimercaprol therapy been tried?

DR. HERMAN BEERMAN: There has been a great deal of interest in tattooing. Dr. Mescon and I have seen a section showing a granulomatous reaction at the site of one of the colors. This section tonight shows nothing that would make one think of a raised lesion. I would suggest that another biopsy specimen be obtained.

CAPT. R. L. GILMAN (MC), U.S.N.: I have seen three or four reactions like this, a pseudokeloid reaction in the cinnabar area. When pathologic processes in tattoo marks are seen, one should consider leprosy, the vagaries of syphilitic reactions, and mercury sensitization. I do not know why this patient should suddenly show a sensitization to mercury; he had no previous history of such sensitization, and yet the reaction to the patch test with ammoniated mercury was positive. In all of the cases studied, the cinnabar area of a tattoo mark has been involved.

DR. IRA L. SCHAMBERG: I should like to suggest that this patient was sensitized to mercury by the injection of cinnabar. Gummatous lesions of syphilis may appear in the nonred areas of a tattoo mark, the red areas not being involved because of the presence of mercury.

Poikiloderma Atrophicans Vasculare (Jacobi). Presented by DR. DOUGLASS A. DECKER, Allentown.
Lichen Planus with Nail Changes; Late Latent Syphilis, Adequately Treated. Presented by DR. H. E. TWINING and DR. CARROLL F. BURGOON.
Keratoderma Palmaris; Psoriasis(?). Presented by DR. H. E. TWINING
Lichen Spinulosus in Sisters. Keratosis Pilaris(?). Presented by DR. HENRY H. PERLMAN.
Purpura Annularis Telangiectodes (Majocchi's Disease). Presented by LT. J. F. MORREL, (MC) U. S. N. (from the service of CAPT. R. L. GILMAN, United States Naval Hospital).
Multiple Neurofibromatosis. Presented by DR. H. E. TWINING, DR. CARROLL F. BURGOON JR., and (by invitation) DR. L. CHUNN.
Discoid Lupus Erythematosus(?). Presented by DR. CARROLL F. BURGOON JR.
Alopecia Associated with Secondary Syphilis. Presented by DR. H. E. TWINING and DR. CARROLL F. BURGOON JR.
Fixed Drug Eruption Due to Sulfadiazine. Presented by DR. H. E. TWINING.
Generalized Disseminated Psoriasis. Presented by DR. H. H. PERLMAN.
Lichen Planus. Presented by DR. H. E. TWINING, DR. CARROLL F. BURGOON JR., and (by invitation) DR. LOUIS JAFFE.
Granuloma Annulare. Presented by DR. H. E. Twining.
Discoid Lupus Erythematosus Profundus. Presented by DR. H. E. TWINING and DR. CARROLL F. BURGOON JR.
Sarcoidosis. B.C.G. Vaccination. Presented by DR. H. E. TWINING and DR. CARROLL F. BURGOON JR.
Alopecia Areata. Presented by DR. CARROLL F. BURGOON JR.
Recurrent Basal Cell Cancer. Presented by DR. H. E. TWINING, DR. CARROLL F. BURGOON JR., and (by invitation) DR. LOUIS JAFFE.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Stuart C. Way, M.D., *President*

Rees B. Rees, M.D., *Secretary*

April 20, 1951

Carcinoma of the Upper Lip, Squamous Cell Type. Presented by DR. ROBERT WALTON (by invitation).

E. C., a 41-year-old white American, first manifested persistent progressive painful swelling and redness of the skin of the upper lip and nose in March, 1950. Two surgical attempts were made at draining what were then considered multiple sebaceous cysts of the nares, and aureomycin and terramycin, administered parenterally, produced no response.

Inspection reveals edema, erythema, and ulceration of the upper lip, extending superiorly to involve both nostrils, with perforation of the internasal septum. There is also edema and erythema of the nose, with ulceration of the upper portion of the nares. The mouth and thorax are normal, and there are no palpable lymph nodes.

Findings from extensive laboratory studies were normal. Roentgenographic studies of the nasal bone, maxilla, and sinuses showed a soft tissue mass in the region of the upper lip, without

evidence of bony invasion. Purulent material from the nose was negative for fungi and showed growth of Escherichia coli and Staphylococcus aureus (coagulase positive). Biopsy of the lip and nose showed squamous cell carcinoma penetrating throughout the cutis.

DISCUSSION

DR. RICHARD SHEPARD (by invitation): At our tumor conference it was considered that chemosurgery would be ideal for this particular problem. Surgical approach or x-ray therapy would be very difficult. This is one of those special problem cases that would seem ideally suited for the Mohs technic. There is also the problem of regional lymph nodes. We have not yet determined whether they are merely inflammatory or whether there is neoplastic involvement. We will treat the primary lesion with chemosurgery and then consider the problem of the nodes later.

DR. EUGENE FARBER: This case has been hard to diagnose. In the past a plastic surgeon had removed a sebaceous cyst from the nose, and subsequently an ear, nose, and throat specialist had treated lesions in this area with fulguration on the assumption that they were sebaceous cysts. Five biopsies were performed by us, only one of which showed positive findings, and this showed a squamous cell epithelioma arising from a cyst wall. I had hoped that x-ray therapy would be possible because chemosurgery would cause such mutilation.

DR. RICHARD SHEPARD: Dr. Newell considers that there is a 50% chance of controlling this process with x-ray therapy but that undoubtedly severe damage would result to the cartilage.

DR. STUART WAY: I feel that x-ray therapy is contraindicated because of the danger of chondrodermatitis.

DR. KEMP DOWDY: Was the carcinoma considered to be primary or secondary and superimposed upon another infection?

DR. HARRY ALDERSON: One must consider the possibility of rhinoscleroma having been present initially.

DR. STUART WAY: We occasionally see rhinoscleroma, but I have never seen carcinoma arise out of it.

DR. HARRY ALDERSON: That is true, but there is always the possibility that it may.

DR. FRANCES KEDDIE: Is the slide on which the diagnosis of squamous cell carcinoma was made the one that was shown tonight? The possibility of infectious granuloma should be considered, and a thorough search made for possible cause of a granuloma.

DR. JOHN SKAHEN (by invitation): Initially we found pseudoepitheliomatous hyperplasia, with the thought that it might be complicating an infectious granuloma. A thorough search was made for fungi, and cultures did not show anything. Regarding the possibility of rhinoscleroma, the particular distinguishing cell found in that disease, called the Mikulicz cell, was not in evidence. The question of pseudoepitheliomatous hyperplasia resolved itself when a diagnosis of squamous cell epithelioma was made. Dr. Nathan Chandler Foote has described epitheliomas arising from hair follicles and skin appendages, in which one may see keratinized cells with intracellular bridges but a growth that looks like and behaves like a basal cell epithelioma.

DR. NORMAN EPSTEIN: Before specific treatment is given for the carcinoma, I believe this patient should be treated for the secondary infection.

DR. EUGENE FARBER: He has been on a long course of terramycin and is sensitive to penicillin. We regret that we have been unable to resolve the stubborn secondary infection. The acute inflammation of the tip of his nose at the present time undoubtedly is due to secondary infection.

Solid Edema of the Upper Lip Treated with Lyophilized Hyaluronidase. Presented by LIEUTENANT COLONEL ROBERT HIGDON, M.C., U. S. A.

N. R., a 37-year-old man, states that a severe edema of the upper lip suddenly developed for the first time in 1942. The edema subsided spontaneously within 10 days. He had no further difficulty until early in November, 1950, when he awoke one morning with a marked swelling of the upper lip.

A histologic section showed a chronic, nonspecific, inflammatory edema, and no organisms were found after prolonged search under oil immersion.

It was decided to treat the patient with local injections of lyophilized hyaluronidase ("wydase," Wyeth, Inc.) into the edematous tissue. Using a dilution of 150 turbidity-reducing units dissolved in 25 cc. of sterile isotonic sodium chloride solution, a total of 9 cc., containing 54 turbidity-reducing units was injected at four sites in the upper lip. The next day a definite decrease in size of the patient's lip was seen. On Feb. 11, 1951, a total of 66 units was similarly injected. During the next 96 hours the lip continued slowly to diminish in size. On Feb. 15 a total of 72 units was injected into the lip, but the patient failed to show as good a response as he had to previous injections. On Feb. 21 the hyaluronidase solution was doubled in concentration by dissolving 150 turbidity-reducing units in 12 cc. of sterile isotonic sodium chloride solution. Seventy-two units of this solution were injected on that date into the same four sites of the patient's upper lip, and he improved so markedly that no further treatment was given for one week. On Feb. 28 a total of 150 units of the same concentration was administered. Since this injection the patient's lip has continued to show a slow but steady decrease in size, despite the fact that no treatment has been given for the past 16 days.

DISCUSSION

DR. FREDERICK NOVY JR.: I have been following this case, and I believe that the diagnosis is correct. As I recall, he has been given antibiotics and other therapy without success. Thorough considerations have been given to it also, such as the possibility of allergy. Hyaluronidase was started. The results have been definite, even more than the photos would indicate. This approach, if successful, would be much better than injection of boiling water and other forms of treatment that have been suggested.

DR. GORDON EKBLAD: We have had one patient with solid edema of the cheek at Oak Knoll Naval Hospital who did not respond to injections of hyaluronidase.

DR. NORMAN EPSTEIN: I believe this should be considered as a form of localized elephantiasis rather than as localized myxedema or some such disease. It is suggestive of an infectious process with a lymphatic block.

DR. HARRY ALDERSON: Do these conditions ever involute without treatment? I know a well-known merchant in San Francisco who had pronounced involvement and who happens to be an ardent Christian Scientist. His lymphedema has disappeared during the past year.

DR. STUART WAY: I think the course of the disease depends upon the cause.

DR. JOHN GRAVES: The patient seems to have answered that question himself. He informed me that he had a similar attack some years ago which cleared without treatment.

LIEUTENANT COLONEL ROBERT HIGDON, M.C., U. S. A.: We consider this to be an example of lymphedema, or solid edema, and not myxedema. We will continue to observe him and to see how long the improvement will last.

Solar Dermatitis (Plaque Type). Presented by DR. BERNARD RYAN.

This 52-year-old white man has been a patient at the Livermore Veterans' Administration Hospital since 1942, shortly after a diagnosis of pulmonary tuberculosis was made. A roentgenogram revealed pulmonary tuberculosis involving all the lobes of both lungs, with cavity formation in the right and left upper lobes. The sputum at that time was positive for acid-fast bacilli and has remained so ever since.

During his nine years of hospitalization, numerous mechanical procedures, such as pneumothorax, phrenic crush, and pneumoperitoneum were done, without converting the sputum. In December, 1948, streptomycin on an interrupted regimen (1.0 gm. every five days) was given, also without converting the sputum. During the past two years he has been considered a "good chronic" and has had no significant complaints referable to his chest. He has been ambulatory and has been kept in the hospital essentially as a domiciliary patient. During the summer months he spends one or two hours each day sitting in the sunshine without a hat.

In the early part of 1949, irregular patches of an erythematous nature were discovered symmetrically on the temples, and the patient states that they became more "inflamed" after exposure to sun. He was seen for the first time by a dermatologist on April 20, 1950, at which time these lesions were described as grossly symmetrical, nonsymptomatic (except for periodic burning sensations) irregular patches of erythema with superficial atrophy, fine silvery scaling,

telangiectasia, and hyperpigmentation. In addition, the skin showed only minimal seborrheic scaling of the scalp. His blood pressure at that time was 180 mm. of mercury systolic and 110 mm. of mercury diastolic; otherwise, there were no significant physical findings except for his lungs. The laboratory data at the time were as follows: a white blood count of 12,500, with 43% neutrophils, 54% lymphocytes, and 3% eosinophils; red blood count of about 5,000,000, and hemoglobin of 95%. Sedimentation rate was 24 mm. per hour. Results of urinalysis were essentially normal. Kahn and Wassermann tests elicited negative reactions.

During the past five months these lesions have faded slowly to a dull-brownish hue, with loss of a good part of the original bright-red erythema. However, there has been no regression in the extent of the lesions.

Local treatment has consisted of 4% ichthammol N. F. (ichthyol®) in zinc oxide ointment.

A punch biopsy of one of the lesions is shown.

DISCUSSION OF TWO PRECEDING CASES

DR. NORMAN EPSTEIN: I believe this case is more compatible with solar eczema than the case presented by Dr. Herman Allington. The distinction between chronic discoid lupus erythematosus and this condition may be very difficult to make at times.

DR. PATRICK BUTLER: This patient has been in a Veterans' Administration hospital with tuberculosis for many years. While these patients are at absolute bed rest, their only amusement is to listen to the radio with ear phones. They acquire the habit of resting the ear phone partially on their cheek. These appliances are made of bakelite, a phenolic resin. One, therefore, may consider the possibility of a berloque-type of photosensitization following his hospital release and subsequent increased exposure to sunlight.

DR. BERNARD RYAN: When I first saw this patient I considered it to be discoid lupus erythematosus and treated him with injections of a bismuth preparation. At that time the summer was about over, and the favorable response to treatment was mistakenly attributed to the bismuth preparation. However, the condition flared up again on reexposure to sunlight. The biopsy findings were at first thought to be compatible with chronic discoid lupus erythematosus. Dr. Fasal thought that it was not chronic discoid lupus erythematosus, and the sections were then sent to Dr. Hamilton Montgomery, who also considered the histologic findings to be incompatible with chronic discoid lupus erythematosus. He believed the histologic changes to be those of a solar dermatitis. Certainly it is true that it is oftentimes impossible to make an accurate distinction, either grossly or histologically, between these two entities.

Inoculation Tuberculosis of the Skin. Presented by DR. KEMP DOWDY.

T. H., a 34-year-old, California-born Japanese man, is a "serviceman" for aquariums, handling goldfish and other types of tropical marine life. In September, 1950, he received a minor laceration on the dorsum of the left third finger, middle phalanx, by a cut from a piece of glass which he was preparing for an aquarium.

Initial examination was done Jan. 17, 1951, approximately five months subsequent to the initial injury. He presented large, nontender, fluctuant abscesses of the hand, forearm, and arm. There were many shot-like, subcutaneous nodules surrounding the left third finger, extending over the dorsum of the hand, the medial surface of the forearm, the epitrochlear space, and axilla. There was a mild, lichenified eczema covering the area of the original injury. The clinical appearance of this eruption initially suggested sporotrichosis.

An extensive examination was done: repeated nodule biopsy, sporotrichin skin test, and cultures on Sabouraud's media and blood agar of the fluid obtained from the subcutaneous abscesses. Mouse inoculations were also done. All findings were repeatedly normal. A specimen of skin was recently taken for biopsy from the involved area of the left third finger. Pathologic studies were done by Dr. Wilbert Sachs. Pathologic examination of the nodules were suggestive of tuberculosis but not diagnostic. There have been a few granules noted on close examination of the sections but no true tuberculous organisms. Reaction to tuberculin skin tests was moderately positive. Results of general physical examination were normal. A roentgenogram of the chest disclosed no pathologic findings suggestive of tuberculosis.

Dr. Wilbert Sachs's report on the pathology is as follows: The diagnosis is tuberculosis cutis. I believe this may have been an inoculation tuberculosis. Throughout the cutis are numerous,

dilated blood vessels and a cellular reaction. The overlying epidermis is enormously irregularly acanthotic. For the most part the surface is verrucous and covered with an increased horny layer; beneath this the granular layer is also increased. In some areas the palisade layer is missing, and in other zones the palisade layer is intact. Otherwise, there are no important changes within the epidermis. The cellular infiltration is composed chiefly of small, round, and wandering connective tissue cells. There are many epithelioid cells; an occasional giant cell is noted. In several areas there appears to be tubercle formation. This picture does not impress me as any type of fungus or beryllium granuloma.

DISCUSSION

DR. KEMP DOWDY: I understand that there is a form of tuberculosis which is encountered in fish, and various textbooks on the subject mention it. However, this particular disease has never been known to infect man. If the organism is inoculated into a guinea pig, it will die rapidly.

DR. FRANCES TORREY: Have organisms been found in an acid-fast stain?

DR. KEMP DOWDY: No. The diagnosis was made on clinical grounds with the presence of the cold abscesses.

A Case for Diagnosis (Allergic Contact Dermatitis with Secondary Hypertrophic Scar Formation?). Presented by DR. KEMP DOWDY.

Solar Eczema. Presented by DR. HERMAN ALLINGTON.

A Case for Diagnosis (Acnitis). Presented by DR. ARNE INGELS.

Obituaries

DUDLEY CROFFORD SMITH, M.D.
1892-1950

D. C. Smith died of coronary thrombosis Aug. 30, 1950, while reading quietly in bed in a hotel room in Washington, D.C., where he had stopped on his way home from a meeting in Philadelphia.

He was born in Lafayette Springs, Miss., Dec. 15, 1892, the son of Dr. J. G. M. Smith, a physician, and Carra Powell Smith. He was educated at the Lafayette Springs High School, and received his Bachelor of Science degree at the University of Mississippi in 1914. He graduated with the degree of M.D. at the University of Virginia in 1916. Dr. Smith was intern and resident in medicine at the University of Virginia Hospital, after which he continued as a member of the Medical Department.

It was during this period that he became interested in dermatology, and he spent the summers for a number of years at various clinics, including the Johns Hopkins Hospital, the Barnard Hospital, Charity Hospital of Louisiana in New Orleans, the Graduate Hospital of the University of Pennsylvania, and the Presbyterian Hospital in New York.

In 1924, Dr. Smith founded the University of Virginia's Department of Dermatology and Syphilology, which he headed until his death.

Dr. Smith was an active and enthusiastic member of numerous local, regional, and national medical and dermatological societies, and he was a member of the American Dermatological Association. He was made Chairman-Elect of the Section on Dermatology and Syphilology of the American Medical Association in June, 1950.

In 1921 he married Lake Morrow of Toccopola, Miss. He is survived by his wife, one son, Dudley Crofford Smith Jr., a daughter, Marjorie (Mrs. Hamilton Smithey), his mother, Mrs. Carra Smith, and a sister, Miss Myrtle Smith. Another son, Powell Morrow Smith, died in infancy.

"D. C.," as he was known by everyone, was an approachable and friendly man, with engaging qualities of shyness and modesty. Although he could give a good account of himself at meetings, public speaking was not among his accomplishments, and for this reason he was at his best as a bedside teacher, and as a director of graduate study and research. By training and experience Dr. Smith was a "medical dermatologist," and this was emphasized in his teachings. His stimulating staff conferences were a delight to all of his graduate students.

His only hobby was his work. Occasionally he went on fishing trips, which he enjoyed immensely, but these were infrequent, and he went less often in his last years.

D. C. enjoyed professional meetings, and there were few at which he was not present. There he would oftentimes be seen surrounded by a devoted group of his students, his thumbs tucked in his vest, one foot forward, and displaying the characteristic arched eyebrow and wide grin.

Sensitive about the feelings of others, D. C. was gentle and tactful in speech, but he could be uncompromising about issues on which he had strong convictions. He was intolerant of deceit and dishonesty, and there were occasions upon which he was outspoken in his contempt for those in whom he detected lack of integrity. He loved comfort, and the good things of life, but he lived without ostentation.

D. C. Smith's primary interest in syphilis is reflected in his many publications. He was interested especially in the epidemiology of syphilis and made a number

DUDLEY CROFFORD SMITH, M.D.
1892-1950

of significant contributions to the understanding of this important public health matter. He wrote extensively on the penicillin treatment of syphilis. He particularly enjoyed his work as a Special Consultant to the United States Public Health Service, which he served from 1933 until his death.

Alone, and in collaboration with his associates, he published a number of papers on various aspects of dermatology, including the cutaneous manifestations of tularemia and sprue, acanthosis nigricans, mycosis fungoides, and artificial fever therapy.

Physically, D. C. Smith was slender and youthful in appearance. Although not physically robust, he was capable of tremendous endurance, and was a hard and indefatigable worker. Depleted by the heavy work-load during the war years, by the incessant demands on his time, and by the inroads on his slender reserves of physical strength, he rarely complained, and then only of vague fatigue. In his last years, he made attempts to get more rest and to distribute the burden of teaching, research, and practice among his subordinates. His tremendous interests and obligations, however, prevented his being completely successful in this.

His loss, at the height of his career, and without warning, left everyone who knew him with a feeling of deep personal loss.

D. C. Smith's personality was a blend of kindliness and wisdom, generosity, and complete unselfishness. He was unfailingly loyal to his profession, his specialty, and his students. He was above all else, a good clinical physician in the Osler tradition, and he will be well remembered.

WILLIAM H. KAUFMAN, M.D.

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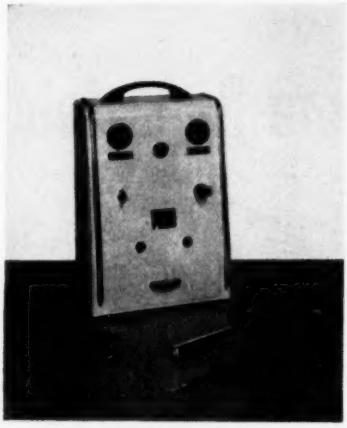

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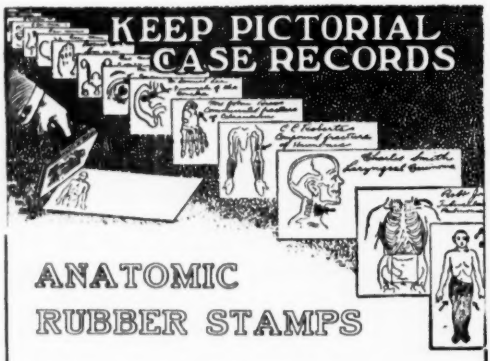

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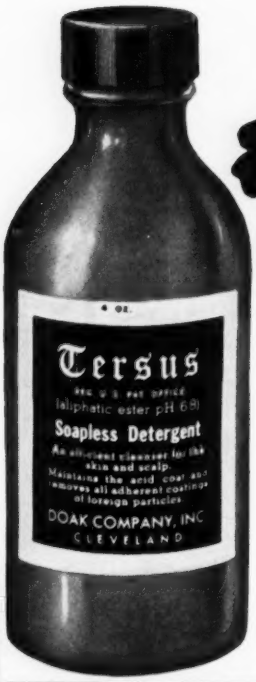

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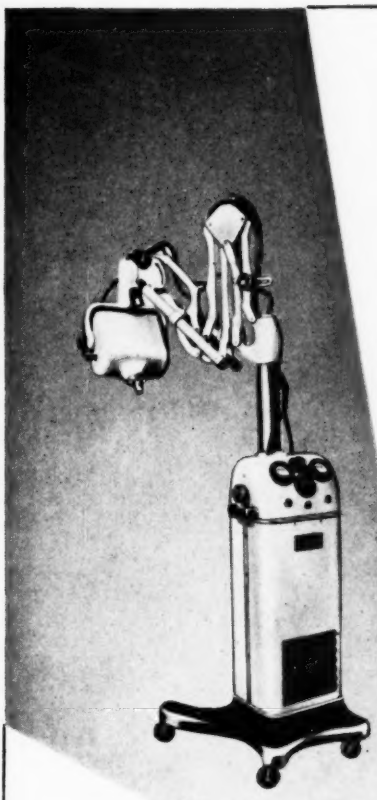

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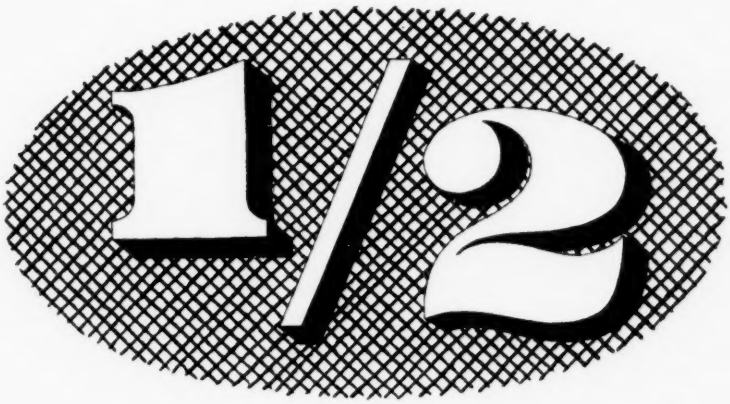

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